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=> e andersen peter/au
E1            6     ANDERSEN PERNILLE/AU
E2            1     ANDERSEN PETE/AU
E3          329 --> ANDERSEN PETER/AU
E4            4     ANDERSEN PETER A/AU
E5            1     ANDERSEN PETER ANDREAS/AU
E6            5     ANDERSEN PETER B/AU
E7           59     ANDERSEN PETER C/AU
E8            1     ANDERSEN PETER CHRISTIAN/AU
E9            3     ANDERSEN PETER CRAIG/AU
E10          62     ANDERSEN PETER E/AU
E11           1     ANDERSEN PETER ESKIL/AU
E12           1     ANDERSEN PETER ESKILD/AU

=> s e3-e12 and tuberculosis
L1          236 ("ANDERSEN PETER"/AU OR "ANDERSEN PETER A"/AU OR "ANDERSEN PETER
                 ANDREAS"/AU OR "ANDERSEN PETER B"/AU OR "ANDERSEN PETER C"/AU
                OR "ANDERSEN PETER CHRISTIAN"/AU OR "ANDERSEN PETER CRAIG"/AU
                OR "ANDERSEN PETER E"/AU OR "ANDERSEN PETER ESKIL"/AU OR "ANDERS
                EN PETER ESKILD"/AU) AND TUBERCULOSIS

=> dup rem l1
PROCESSING COMPLETED FOR L1
L2           124 DUP REM L1 (112 DUPLICATES REMOVED)

=> s l2 and (rd1?
UNMATCHED LEFT PARENTHESIS 'AND (RD1?'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s l2 and (rd1?)
L3           14 L2 AND (RD1?)

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YOU HAVE REQUESTED DATA FROM 14 ANSWERS - CONTINUE? Y/(N):y
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L3 ANSWER 1 OF 14 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2004:345624 BIOSIS
DN PREV200400347773
TI Reactivation of **tuberculosis** during immunosuppressive treatment in a patient with a positive QuantiFERON(R)-**RD1** Test.
AU Ravn, Pernille [Reprint Author]; Munk, Martin E.; Andersen, Ase Bengaard; Lundgren, Bettina; Nielsen, Lars N.; Lillebaek, Troels; Soerensen, Inge J.; **Andersen, Peter**; Weldingh, Karin
CS Hvidovre HospDept Infect Dis, Univ Copenhagen, Kettegards Alle 30, DK-2650, Hvidovre, Denmark
pravn@dadlnet.dk
SO Scandinavian Journal of Infectious Diseases, (July 2004) Vol. 36, No. 6-7, pp. 499-501, 497. print.
CODEN: SJIDB7. ISSN: 0036-5548.
DT Article
LA English
ED Entered STN: 18 Aug 2004
Last Updated on STN: 18 Aug 2004
AB A patient with polymyositis developed **tuberculosis** during immunosuppressive treatment. Tuberculin Skin Test and chest X-ray failed to demonstrate latent **tuberculosis**, whereas a blood sample that was tested with a modified QuantiFERON(R)-TB-assay, using the recombinant ESAT-6 and CFP-10, was positive indicating that this patient was latently infected before immunosuppressive therapy. This case indicates the risk of progressing from latent to active **tuberculosis** given that the subject is **RD1** responsive, and we believe that preventive anti-tuberculous treatment could have prevented this case of **tuberculosis**. We suggest that **RD1** based tests are evaluated further in immunocompromised patients.
TI Reactivation of **tuberculosis** during immunosuppressive treatment in a patient with a positive QuantiFERON(R)-**RD1** Test.
AU . . Ravn, Pernille [Reprint Author]; Munk, Martin E.; Andersen, Ase Bengaard; Lundgren, Bettina; Nielsen, Lars N.; Lillebaek, Troels; Soerensen, Inge J.; **Andersen, Peter**; Weldingh, Karin
AB A patient with polymyositis developed **tuberculosis** during immunosuppressive treatment. Tuberculin Skin Test and chest X-ray failed to demonstrate latent **tuberculosis**, whereas a blood sample that was tested with a modified QuantiFERON(R)-TB-assay, using the recombinant ESAT-6 and CFP-10, was positive indicating. . . that this patient was latently infected before immunosuppressive therapy. This case indicates the risk of progressing from latent to active **tuberculosis** given that the subject is **RD1** responsive, and we believe that preventive anti-tuberculous treatment could have prevented this case of **tuberculosis**. We suggest that **RD1** based tests are evaluated further in immunocompromised patients.
IT . . .
and Homeostasis); Infection; Methods and Techniques
IT Parts, Structures, & Systems of Organisms
blood: blood and lymphatics, analysis
IT Diseases
tuberculosis: bacterial disease, diagnosis, etiology
Tuberculosis (MeSH)
IT Methods & Equipment
QuantiFERON-**RD1** test: clinical techniques, diagnostic techniques, laboratory techniques; immunosuppresive therapy: clinical techniques, immunologic techniques, laboratory techniques, therapeutic and prophylactic techniques; tuberculin. . .
ORGN . . .
Mammals, Primates, Vertebrates
ORGN Classifier
Mycobacteriaceae 08881
Super Taxa
Mycobacteria; Actinomycetes and Related Organisms; Eubacteria; Bacteria; Microorganisms
Organism Name
Mycobacterium **tuberculosis** (species): pathogen
Taxa Notes
Bacteria, Eubacteria, Microorganisms

L3 ANSWER 2 OF 14 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2004:76163 BIOSIS
DN PREV200400078267
TI Human T-cell responses to the **RD1**-encoded protein TB27.4 (Rv3878) from Mycobacterium **tuberculosis**.
AU Agger, Else Marie [Reprint Author]; Brock, Inger; Okkels, Limei Meng; Arend, Sandra M.; Aagaard, Claus S.; Weldingh, Karin N.; **Andersen, Peter**
CS Department of Infectious Disease Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen, S, Denmark
eag@ssi.dk
SO Immunology, (December 2003) Vol. 110, No. 4, pp. 507-512. print.
CODEN: IMMUAM. ISSN: 0019-2805.
DT Article
LA English
ED Entered STN: 4 Feb 2004
Last Updated on STN: 4 Feb 2004
AB In recent years, there has been considerable focus on the discovery and characterization of proteins derived from Mycobacterium **tuberculosis** leading to the identification of a number of candidate antigens for use in vaccine development or for diagnostic purposes. Previous experiments have demonstrated an important immunological role for proteins encoded by the **RD1** region, which is absent from all strains of bacillus Calmette-Guerin (BCG) but present in the genomes of virulent M. bovis and M. **tuberculosis**. Herein, we have studied human T-cell responses to the antigen encoded by the putative open reading frame (rv3878) of the **RD1** region. Immunoblot analysis revealed that rv3878 was expressed and the native protein was designated TB27.4. Immunological evaluations demonstrate that TB27.4 elicits a prominent immune response in human **tuberculosis** patients with a dominant region in the C-terminal part of the molecule. In contrast, very limited responses were seen in M. bovis BCG-vaccinated donors. This study therefore emphasizes the diagnostic potential of proteins encoded by the **RD1** region.
TI Human T-cell responses to the **RD1**-encoded protein TB27.4 (Rv3878) from Mycobacterium **tuberculosis**.
AU Agger, Else Marie [Reprint Author]; Brock, Inger; Okkels, Limei Meng; Arend, Sandra M.; Aagaard, Claus S.; Weldingh, Karin N.; **Andersen, Peter**
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IT . . .
T-cell: blood and lymphatics, immune system
IT Diseases
Mycobacterium bovis infection: bacterial disease, infectious disease
Mycobacterium Infections (MeSH)
IT Diseases
Mycobacterium **tuberculosis** infection: bacterial disease, infectious disease
Mycobacterium Infections (MeSH)
IT Chemicals & Biochemicals
BCG vaccine: immunologic-drug, immunostimulant-drug; TB27.4:

RD1-encoded protein
ORGN . . .
ORGN Classifier
Mycobacteriaceae 08881
Super Taxa
Mycobacteria; Actinomycetes and Related Organisms; Eubacteria;
Bacteria; Microorganisms
Organism Name
Mycobacterium bovis (species): pathogen
Mycobacterium **tuberculosis** (species): pathogen
Taxa Notes
Bacteria, Eubacteria, Microorganisms
GEN Mycobacterium **tuberculosis** rv3878 gene (Mycobacteriaceae): expression

L3 ANSWER 3 OF 14 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2004:33002 BIOSIS
DN PREV200400035432
TI PPE protein (Rv3873) from DNA segment **RD1** of Mycobacterium **tuberculosis**: Strong recognition of both specific T-cell epitopes and epitopes conserved within the PPE family.
AU Okkels, Limei Meng [Reprint Author]; Brock, Inger; Follmann, Frank; Agger, Else Marie; Arend, Sandra M.; Ottenhoff, Tom H. M.; Oftung, Fredrik; Rosenkrands, Ida; **Andersen, Peter**
CS Department of Infectious Disease Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen, Denmark
lmo@ssi.dk
SO Infection and Immunity, (November 2003) Vol. 71, No. 11, pp. 6116-6123. print.
ISSN: 0019-9567 (ISSN print).
DT Article
LA English
ED Entered STN: 7 Jan 2004
Last Updated on STN: 7 Jan 2004
AB Proteins encoded by DNA segment **RD1** of Mycobacterium **tuberculosis** have recently been demonstrated to play important roles in bacterial virulence, vaccine development, and diagnostic reagent design. Previously, we characterized two immunodominant T-cell antigens, the early secreted antigen target (ESAT-6),and the 10-kDa culture filtrate protein (CFP10), which are encoded by the esx-1hp operon in this region. In the present study we characterized a third putative open reading frame in this region, rv3873, which encodes a PPE protein. We found that the rv3873 gene is expressed in M. **tuberculosis** H37Rv and that the native protein, Rv3873, is predominantly associated with the mycobacterial cell or wall. When tested as a His-tagged recombinant protein, Rv3873 stimulated high levels of gamma interferon secretion in peripheral blood mononuclear cells isolated from **tuberculosis** (TB) patients, as well as from healthy tuberculin purified protein derivative-positive donors. In contrast to other **RD1**-encoded antigens, Rv3873 was also found to be recognized by a significant proportion of Mycobacterium bovis BCG-vaccinated donors. Epitope mapping performed with overlapping peptides revealed a broad pattern of T-cell recognition comprising both TB-specific epitopes and epitopes also recognized by BCG-vaccinated donors. The immunodominant epitope (residues 118 to 1.35) for both TB patients and BCG-vaccinated individuals was found to be highly conserved among a large number of PPE family members.
TI PPE protein (Rv3873) from DNA segment **RD1** of Mycobacterium **tuberculosis**: Strong recognition of both specific T-cell epitopes and epitopes conserved within the PPE family.
AU. . . [Reprint Author]; Brock, Inger; Follmann, Frank; Agger, Else Marie; Arend, Sandra M.; Ottenhoff, Tom H. M.; Oftung, Fredrik; Rosenkrands, Ida; **Andersen, Peter**
AB Proteins encoded by DNA segment **RD1** of Mycobacterium **tuberculosis** have recently been demonstrated to play important roles in bacterial virulence, vaccine development, and diagnostic reagent design. Previously, we characterized. . . frame in this region, rv3873, which encodes a PPE protein. We found that the rv3873 gene is expressed in M. **tuberculosis** H37Rv and that the native protein,

Rv3873, is predominantly associated with the mycobacterial cell or wall. When tested as a His-tagged recombinant protein, Rv3873 stimulated high levels of gamma interferon secretion in peripheral blood mononuclear cells isolated from **tuberculosis** (TB) patients, as well as from healthy tuberculin purified protein derivative-positive donors. In contrast to other **RD1**-encoded antigens, Rv3873 was also found to be recognized by a significant proportion of Mycobacterium bovis BCG-vaccinated donors. Epitope mapping performed. . .

IT . . .
and Homeostasis)

IT Parts, Structures, & Systems of Organisms
peripheral blood mononuclear cell: blood and lymphatics, immune system

IT Diseases
tuberculosis: bacterial disease, infectious disease
Tuberculosis (MeSH)

IT Chemicals & Biochemicals
DNA segment **RD1**; PPE protein; T-cell antigens; T-cell epitopes; culture filtrate protein 10 [CFP10]; early secreted antigen target 6 [ESAT-6]; epitopes; esx-1hp operon;. . .

ORGN Classifier
Mycobacteriaceae 08881

Super Taxa
Mycobacteria; Actinomycetes and Related Organisms; Eubacteria; Bacteria; Microorganisms

Organism Name
Mycobacterium **tuberculosis** (species): strain-H37Rv

Taxa Notes
Bacteria, Eubacteria, Microorganisms

GEN Mycobacterium **tuberculosis** rv3873 gene (Mycobacteriaceae)

L3 ANSWER 4 OF 14 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

AN 2000:282183 BIOSIS

DN PREV200000282183

TI Antigenic equivalence of human T-cell responses to Mycobacterium **tuberculosis**-specific **RD1**-encoded protein antigens ESAT-6 and culture filtrate protein 10 and to mixtures of synthetic peptides.

AU Arend, Sandra M. [Reprint author]; Geluk, Annemieke; van Meijgaarden, Krista E.; van Dissel, Jaap T.; Theisen, Michael; **Andersen, Peter**; Ottenhoff, Tom H. M.

CS Department of Infectious Diseases, C5P, Leiden University Medical Center, 2300 RC, Leiden, Netherlands

SO Infection and Immunity, (June, 2000) Vol. 68, No. 6, pp. 3314-3321. print. CODEN: INFIBR. ISSN: 0019-9567.

DT Article

LA English

ED Entered STN: 6 Jul 2000
Last Updated on STN: 7 Jan 2002

AB The early secreted antigenic target 6-kDa protein (ESAT-6) and culture filtrate protein 10 (CFP-10) are promising antigens for reliable immunodiagnosis of **tuberculosis**. Both antigens are encoded by **RD1**, a genomic region present in all strains of Mycobacterium **tuberculosis** and M. bovis but lacking in all M. bovis bacillus Calmette-Guerin vaccine strains. Production and purification of recombinant antigens are laborious and costly, precluding rapid and large-scale testing. Aiming to develop alternative diagnostic reagents, we have investigated whether recombinant ESAT-6 (rESAT-6) and recombinant CFP-10 can be replaced with corresponding mixtures of overlapping peptides spanning the complete amino acid sequence of each antigen. Proliferation of M. **tuberculosis**-specific human T-cell lines in response to rESAT-6 and rCFP-10 and that in response to the corresponding peptide mixtures were almost completely correlated ($r = 0.96$, $P < 0.0001$ for ESAT-6; $r = 0.98$, $P < 0.0001$ for CFP-10). More importantly, the same was found when gamma interferon production by peripheral blood mononuclear cells in response to these stimuli was analyzed ($r = 0.89$, $P < 0.0001$ for ESAT-6; $r = 0.89$, $P < 0.0001$ for CFP-10). Whole protein antigens and the peptide mixtures resulted in identical sensitivity and specificity for detection of infection with M. **tuberculosis**. The peptides in

DT Article
LA English
OS Genbank-AF004671
ED Entered STN: 3 Feb 1999
Last Updated on STN: 3 Feb 1999
AB The early secreted antigenic target 6 kDa protein (ESAT-6) is a potent T-cell protein antigen synthesized by Mycobacterium **tuberculosis**. Its corresponding gene (esat-6) is located in **RD1**, a 10 kb DNA region deleted in the attenuated **tuberculosis** vaccine strain Mycobacterium bovis BCG. The promoter region of M. **tuberculosis** esat-6 was cloned and characterized. A new gene, designated lhp and cotranscribed with esat-6, was identified. Moreover, computer searches in the M. **tuberculosis** genome identified 13 genes related to the lhp/esat-6 operon, defining a novel gene family. The transcription initiation sites of the lhp/esat-6 operon were mapped using M. **tuberculosis** RNA. The corresponding promoter signals were not recognized in Mycobacterium smegmatis, in which transcription of lhp/esat-6 is initiated at different locations. The M. **tuberculosis** lhp gene product was identified as CFP-10, a low-molecular-mass protein found in the short-term culture filtrate. These results show that the genes encoding CFP-10 and ESAT-6 are transcribed together in M. **tuberculosis** and that both code for small exported proteins.
TI A Mycobacterium **tuberculosis** operon encoding ESAT-6 and a novel low-molecular-mass culture filtrate protein (CFP-10).
AU Berthet, Fancois-Xavier [Reprint author]; Rasmusse, Peter Birk; Rosenkrands, Ida; **Andersen, Peter**; Gicquel, Brigitte
AB The early secreted antigenic target 6 kDa protein (ESAT-6) is a potent T-cell protein antigen synthesized by Mycobacterium **tuberculosis**. Its corresponding gene (esat-6) is located in **RD1**, a 10 kb DNA region deleted in the attenuated **tuberculosis** vaccine strain Mycobacterium bovis BCG. The promoter region of M. **tuberculosis** esat-6 was cloned and characterized. A new gene, designated lhp and cotranscribed with esat-6, was identified. Moreover, computer searches in the M. **tuberculosis** genome identified 13 genes related to the lhp/esat-6 operon, defining a novel gene family. The transcription initiation sites of the lhp/esat-6 operon were mapped using M. **tuberculosis** RNA. The corresponding promoter signals were not recognized in Mycobacterium smegmatis, in which transcription of lhp/esat-6 is initiated at different locations. The M. **tuberculosis** lhp gene product was identified as CFP-10, a low-molecular-mass protein found in the short-term culture filtrate. These results show that the genes encoding CFP-10 and ESAT-6 are transcribed together in M. **tuberculosis** and that both code for small exported proteins.
IT Major Concepts
Bacteriology; Infection; Molecular Genetics (Biochemistry and Molecular Biophysics)
IT Diseases
tuberculosis: bacterial disease
Tuberculosis (MeSH)
IT Chemicals & Biochemicals
early secreted antigenic target 6 kDA protein [ESAT-6]: T-cell protein antigen; CFP-10 protein: identification, low-molecular-mass culture filtrate protein; Mycobacterium **tuberculosis** esat-6 gene [early secreted antigenic target 6 kDa protein gene]: characterization, transcription, promoter region, operon, cloning; Mycobacterium **tuberculosis** lhp gene: identification, operon, transcription
ORGN . . .
Mycobacteriaceae 08881
Super Taxa
Mycobacteria; Actinomycetes and Related Organisms; Eubacteria; Bacteria; Microorganisms
Organism Name
Mycobacterium bovis: strain-BCG, vaccine strain
Mycobacterium smegmatis
Mycobacterium **tuberculosis**: pathogen
Taxa Notes

each mixture contributing to the overall response varied between individuals with different HLA-DR types. Interestingly, responses to CFP-10 were significantly higher in the presence of HLA-DR15, which is the major subtype of DR2. These results show that mixtures of synthetic overlapping peptides have potency equivalent to that of whole ESAT-6 and CFP-10 for sensitive and specific detection of infection with M. **tuberculosis**, and peptides have the advantage of faster production at lower cost.

TI Antigenic equivalence of human T-cell responses to Mycobacterium **tuberculosis**-specific **RD1**-encoded protein antigens ESAT-6 and culture filtrate protein 10 and to mixtures of synthetic peptides.

AU Arend, Sandra M. [Reprint author]; Geluk, Annemieke; van Meijgaarden, Krista E.; van Dissel, Jaap T.; Theisen, Michael; **Andersen, Peter**; Ottenhoff, Tom H. M.

AB . . . early secreted antigenic target 6-kDa protein (ESAT-6) and culture filtrate protein 10 (CFP-10) are promising antigens for reliable immunodiagnosis of **tuberculosis**. Both antigens are encoded by **RD1**, a genomic region present in all strains of Mycobacterium **tuberculosis** and M. bovis but lacking in all M. bovis bacillus Calmette-Guerin vaccine strains. Production and purification of recombinant antigens are. . . be replaced with corresponding mixtures of overlapping peptides spanning the complete amino acid sequence of each antigen. Proliferation of M. **tuberculosis**-specific human T-cell lines in response to rESAT-6 and rCFP-10 and that in response to the corresponding peptide mixtures were almost. . . CFP-10). Whole protein antigens and the peptide mixtures resulted in identical sensitivity and specificity for detection of infection with M. **tuberculosis**. The peptides in each mixture contributing to the overall response varied between individuals with different HLA-DR types. Interestingly, responses to. . . peptides have potency equivalent to that of whole ESAT-6 and CFP-10 for sensitive and specific detection of infection with M. **tuberculosis**, and peptides have the advantage of faster production at lower cost.

IT . . .
System (Chemical Coordination and Homeostasis); Infection

IT Parts, Structures, & Systems of Organisms
T-cell; peripheral blood mononuclear cell

IT Diseases
tuberculosis
Tuberculosis (MeSH)

IT Chemicals & Biochemicals
HLA-DR; culture filtrate protein-10; early secreted antigenic target 6-kDa

ORGN . . .
Mammals, Primates, Vertebrates

ORGN Classifier
Mycobacteriaceae 08881

Super Taxa
Mycobacteria; Actinomycetes and Related Organisms; Eubacteria; Bacteria; Microorganisms

Organism Name
Mycobacterium **tuberculosis**

Taxa Notes
Bacteria, Eubacteria, Microorganisms

L3 ANSWER 5 OF 14 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

AN 1999:28278 BIOSIS

DN PREV199900028278

TI A Mycobacterium **tuberculosis** operon encoding ESAT-6 and a novel low-molecular-mass culture filtrate protein (CFP-10).

AU Berthet, Fancois-Xavier [Reprint author]; Rasmusse, Peter Birk; Rosenkrands, Ida; **Andersen, Peter**; Gicquel, Brigitte

CS Unite Geneitque Mycobacteriene, Inst. Pasteur, 25 rue Dr Roux, 75724 Paris Cedex 15, France

SO Microbiology (Reading), (Nov., 1998) Vol. 144, No. 11, pp. 3195-3203. print.
ISSN: 1350-0872.

Bacteria, Eubacteria, Microorganisms

L3 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:490265 CAPLUS
DN 141:52841
TI Cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis
IN **Andersen, Peter**; Skiot, Rikke; Oettinger, Thomas; Rasmussen, Peter Birk; Rosenkrands, Ida; Weldingh, Karin; Florio, Walter
PA Den.
SO U.S. Pat. Appl. Publ., 109 pp., Cont.-in-part of U.S. 6,641,814.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 10

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004115211	A1	20040617	US 2003-620246	20030715
US 6641814	B1	20031104	US 1998-50739	19980330
EP 1449922	A2	20040825	EP 2004-76605	19980401
EP 1449922	A3	20041117		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY

PRAI DK 1997-376	A	19970402	
US 1997-44624P	P	19970418	
DK 1997-1277	A	19971110	
US 1998-70488P	P	19980105	
US 1998-50739	A2	19980330	
DK 1998-1281	A	19981008	
EP 1998-913536	A3	19980401	

AB The present invention is based on the identification and characterization of a number of M. **tuberculosis** derived antigens, isolated from culture filtrates of T cells from memory immune mice by T cell epitope mapping. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, resp. These antigens are suitable for use in vaccines and in diagnosis of infections.
TI Cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis
IN **Andersen, Peter**; Skiot, Rikke; Oettinger, Thomas; Rasmussen, Peter Birk; Rosenkrands, Ida; Weldingh, Karin; Florio, Walter
AB The present invention is based on the identification and characterization of a number of M. **tuberculosis** derived antigens, isolated from culture filtrates of T cells from memory immune mice by T cell epitope mapping. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, resp. These antigens are suitable for use in vaccines and in diagnosis of infections.
ST sequence Mycobacterium culture filtrate antigen gene; **tuberculosis** vaccine diagnosis Mycobacterium culture filtrate antigen gene
IT 213992-10-0P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(M. **tuberculosis** culture filtrate antigen CFP29 N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)
IT 706035-97-4P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(M. **tuberculosis** culture filtrate antigen CFP30A N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 213992-24-6P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(M. **tuberculosis** culture filtrate antigen CFP30B N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 213992-20-2P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(M. **tuberculosis** culture filtrate antigen CFP50 N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 213992-21-3P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(M. **tuberculosis** culture filtrate antigen CFP7B N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 213992-11-1P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(M. **tuberculosis** culture filtrate antigen CFPSA N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-89-4P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(M. **tuberculosis** culture filtrate antigen CFPSB N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 213992-13-3P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(M. **tuberculosis** culture filtrate antigen CWP32 N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-88-3P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-23-6 706035-25-8 706035-27-0 706035-29-2 706035-31-6
706035-33-8 706035-35-0 706035-37-2 706035-39-4 706035-41-8
706035-43-0 706035-45-2 706035-47-4 706035-49-6 706035-51-0
706035-53-2 706035-55-4 706035-57-6 706035-59-8 706035-61-2
706035-63-4 706035-65-6 706035-67-8 706035-69-0 706035-71-4
706035-73-6 706035-75-8 706035-77-0 706035-79-2 706035-81-6
706035-83-8 706035-85-0

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-87-2
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-22-5 706035-24-7 706035-26-9 706035-28-1 706035-30-5
706035-32-7 706035-34-9 706035-36-1 706035-38-3 706035-40-7
706035-42-9 706035-44-1 706035-46-3 706035-48-5 706035-50-9
706035-52-1 706035-54-3 706035-56-5 706035-58-7 706035-60-1
706035-62-3 706035-64-5 706035-66-7 706035-68-9 706035-70-3
706035-72-5 706035-74-7 706035-76-9 706035-78-1 706035-80-5
706035-82-7 706035-84-9
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-86-1
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706036-03-5 706036-04-6 706036-05-7 706036-06-8 706036-07-9
706036-08-0 706036-09-1 706036-10-4 706036-11-5 706036-12-6
706036-13-7 706036-14-8 706036-15-9 706036-16-0 706036-17-1
706036-18-2 706036-19-3 706036-20-6 706036-21-7 706036-22-8
706036-23-9 706036-24-0 706036-25-1 706036-26-2 706036-27-3
706036-28-4 706036-29-5 706036-30-8 706036-31-9 706036-32-0
706036-33-1 706036-34-2 706036-35-3 706036-36-4 706036-37-5
706036-38-6 706036-39-7 706036-40-0 706036-41-1 706036-42-2
706036-43-3 706036-44-4 706036-45-5 706036-46-6 706036-47-7
706036-48-8 706036-49-9 706036-50-2 706036-51-3 706036-52-4
706036-53-5 706036-54-6 706036-55-7 706036-58-0 706036-59-1
706036-60-4 706036-61-5 706036-62-6 706036-63-7 706036-64-8
706036-65-9 706036-66-0 706036-67-1 706036-68-2 706036-69-3
706036-70-6 706036-71-7 706036-72-8 706036-73-9 706036-74-0
706036-75-1 706036-76-2 706036-77-3 706036-78-4 706036-79-5
RL: PRP (Properties)
(unclaimed nucleotide sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706036-56-8 706036-57-9 706036-80-8 706036-81-9
RL: PRP (Properties)
(unclaimed protein sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as v

SYSTEM LIMITS
EXCEEDED

L3 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:60336 CAPLUS
DN 140:144681
TI Mycobacterium low oxygen-induced antigens and genes for vaccines or diagnostics of **tuberculosis**
IN **Andersen, Peter**; Rosenkrands, Ida; Stryhn, Anette
PA Statens Serum Institut, Den.
SO PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DT Patent

LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004006952	A2	20040122	WO 2003-DK477	20030708
	WO 2004006952	A3	20040318		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1523331	A2	20050420	EP 2003-763613	20030708
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 2004057963	A1	20040325	US 2003-617038	20030711
PRAI	DK 2002-1098	A	20020713		
	US 2002-401725P	P	20020807		
	WO 2003-DK477	W	20030708		

AB The present invention is based on a number of M. **tuberculosis** derived proteins and protein fragments which are induced during the latent stage of infection characterized by low oxygen tension in the microenvironment of the infecting TB-bacteria. The invention is directed to the use of these polypeptides, immunol. active fragments thereof and the genes encoding them for immunol. compns. such as therapeutic vaccines and diagnostic reagents.

TI Mycobacterium low oxygen-induced antigens and genes for vaccines or diagnostics of **tuberculosis**

IN **Andersen, Peter**; Rosenkrands, Ida; Stryhn, Anette

AB The present invention is based on a number of M. **tuberculosis** derived proteins and protein fragments which are induced during the latent stage of infection characterized by low oxygen tension in the microenvironment of the infecting TB-bacteria. The invention is directed to the use of these polypeptides, immunol. active fragments thereof and the genes encoding them for immunol. compns. such as therapeutic vaccines and diagnostic reagents.

ST Mycobacterium **tuberculosis** low oxygen induced antigen gene vaccine diagnostic

; BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(γ; Mycobacterium low oxygen-induced antigens and genes for vaccines or diagnostics of **tuberculosis**)

IT 650674-04-7P 650674-05-8P 650674-06-9P 650674-07-0P 650674-08-1P
650674-09-2P 650674-10-5P 650674-11-6P 650674-12-7P 650674-13-8P
650674-14-9P 650674-15-0P 650674-16-1P 650674-17-2P 650674-18-3P
650674-19-4P 650674-20-7P 650674-21-8P 650674-22-9P 650674-23-0P
650674-24-1P 650674-25-2P 650674-26-3P 650674-27-4P 650674-28-5P
650674-29-6P 650674-30-9P 650674-31-0P 650674-32-1P 650674-33-2P
650674-34-3P 650674-35-4P 650674-36-5P 650674-37-6P 650674-38-7P
650674-39-8P 650674-40-1P 650674-41-2P 650674-42-3P 650674-43-4P
650674-44-5P 650674-45-6P 650674-46-7P 650674-47-8P 650674-48-9P
651361-06-7P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; Mycobacterium low oxygen-induced antigens and genes for vaccines or diagnostics of **tuberculosis**)

IT 7782-44-7, Oxygen, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(low; Mycobacterium low oxygen-induced antigens and genes for vaccines or diagnostics of **tuberculosis**)

IT 650674-49-0P 650674-50-3P 650674-51-4P 650674-52-5P 650674-53-6P
650674-54-7P 650674-55-8P 650674-56-9P 650674-57-0P 650674-58-1P
650674-59-2P 650674-60-5P 650674-61-6P 650674-62-7P 650674-63-8P

650674-64-9P 650674-65-0P 650674-66-1P 650674-67-2P 650674-68-3P
650674-69-4P 650674-70-7P 650674-71-8P 650674-72-9P 650674-73-0P
650674-74-1P 650674-75-2P 650674-76-3P 650674-77-4P 650674-78-5P
650674-79-6P 650674-80-9P 650674-81-0P 650674-82-1P 650674-83-2P
650674-84-3P 650674-85-4P 650674-86-5P 650674-87-6P 650674-88-7P
650674-89-8P 650674-90-1P 650674-91-2P 650674-92-3P 650674-93-4P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; Mycobacterium low oxygen-induced antigens and genes for vaccines or diagnostics of **tuberculosis**)

IT 650674-94-5 650674-95-6 650674-96-7 650674-97-8 650674-98-9
650674-99-0 650675-00-6 650675-01-7 650675-02-8 650675-03-9
650675-04-0 650675-05-1 650675-06-2 650675-07-3 650675-08-4
650675-09-5 650675-10-8 650675-11-9 650675-12-0 650675-13-1
650675-14-2 650675-15-3 650675-16-4 650675-17-5 650675-18-6
650675-19-7 650675-20-0 650675-21-1 650675-22-2 650675-23-3
650675-24-4 650675-25-5 650675-26-6 650675-27-7 650675-28-8
650675-29-9 650675-30-2 650675-31-3 650675-32-4 650675-33-5
650675-34-6 650675-35-7 650675-36-8 650675-37-9 650675-38-0
650675-39-1 650675-40-4 650675-41-5 650675-42-6 650675-43-7
650675-44-8 650675-45-9 650675-46-0 650675-47-1 650675-48-2
650675-49-3 650675-50-6 650675-51-7 650675-52-8 650675-53-9
650675-54-0 650675-55-1 650675-56-2 650675-57-3 650675-58-4
650675-59-5 650675-60-8 650675-61-9 650675-62-0 650675-63-1
650675-64-2 650675-65-3 650675-66-4 650675-67-5 650675-68-6
650675-69-7 650675-70-0 650675-71-1 650675-72-2 650675-73-3
650675-74-4 650675-75-5 650675-76-6 650675-77-7 650675-78-8
650675-79-9 650675-80-2 650675-81-3 650675-82-4 650675-83-5
650675-84-6 650675-85-7
RL: PRP (Properties)
(unclaimed sequence; mycobacterium low oxygen-induced antigens and genes for vaccines or diagnostics o

SYSTEM LIMITS EXCEEDED

L3 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:59568 CAPLUS
DN 140:127185
TI Antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment
IN **Andersen, Peter**; Skjot, Rikke Louise Vinther; Okkels, Li Mei Meng; Brock, Inger; Oettinger, Thomas
PA Den.
SO U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 804,980.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 10

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004013685	A1	20040122	US 2001-872505	20010601
EP 1449922	A2	20040825	EP 2004-76605	19980401
EP 1449922	A3	20041117		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
WO 2001004151	A2	20010118	WO 2000-DK398	20000713
WO 2001004151	A3	20010712		
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

	US 2003147897	A1	20030807	US 2001-804980	20010313
PRAI	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-246191	B2	19981230		
	DK 1999-1020	A	19990713		
	US 1999-144011P	P	19990715		
	US 2000-615947	A2	20000713		
	WO 2000-DK398	A2	20000713		
	US 2001-804980	A2	20010313		
	DK 1993-798	A	19930702		
	US 1993-123182	B2	19930920		
	WO 1994-DK273	A2	19940701		
	US 1995-465640	A1	19950605		
	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	EP 1998-913536	A3	19980401		
	US 1999-289388	B2	19990412		

AB The present invention is based on the identification and characterization of 3 antigens, including Rv2653c, Rv2654c and **RD1**-ORF5, from Mycobacterium **tuberculosis**. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing **tuberculosis** caused by virulent mycobacteria in an animal, including a human being. The invention related to treating **tuberculosis** using antigens isolated from Mycobacterium **tuberculosis**.

TI Antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment

IN **Andersen, Peter**; Skjot, Rikke Louise Vinther; Okkels, Li Mei Meng; Brock, Inger; Oettinger, Thomas

AB The present invention is based on the identification and characterization of 3 antigens, including Rv2653c, Rv2654c and **RD1**-ORF5, from Mycobacterium **tuberculosis**. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing **tuberculosis** caused by virulent mycobacteria in an animal, including a human being. The invention related to treating **tuberculosis** using antigens isolated from Mycobacterium **tuberculosis**.

ST Mycobacterium antigen vaccine **tuberculosis** diagnosis

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**RD1**-ORF5; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Rv2653c; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Rv2654c; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT Mycobacterium bovis
(antigen **RD1**-ORF5 expressed in; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antibodies and Immunoglobulins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT Fusion proteins (chimeric proteins)
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)
(antigens in; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT Animal
Human
(diagnosis of **tuberculosis** in; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT **Tuberculosis**
(diagnosis, **tuberculosis**; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT Diagnosis
(immunodiagnosis; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Drug delivery systems
(injections, intradermally; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antibodies and Immunoglobulins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(monoclonal; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT Epitopes
Molecular cloning
Mycobacterium **tuberculosis**
Tuberculosis
Tuberculostatics
Vaccines
(protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Immunoassay
(skin test; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Diagnosis
(**tuberculosis**, **tuberculosis**; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT Immunization
(vaccination; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Mycobacterium
(virulent; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Interferons
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(γ; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT 649655-13-0 649655-14-1 649655-15-2 649655-16-3 649655-17-4
649655-18-5 649655-19-6 649655-20-9
RL: PRP (Properties)
(unclaimed nucleotide sequence; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT 649655-09-4 649655-10-7 649655-11-8 649655-12-9
RL: PRP (Properties)
(unclaimed protein sequence; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT 649543-98-6 649544-02-5 649544-05-8 649544-08-1 649544-11-6
649544-14-9 649544-18-3 649544-21-8 649544-24-1 649544-27-4
649544-30-9 649544-33-2 649544-36-5 649544-40-1 649544-43-4
649544-46-7 649544-49-0 649544-52-5 649544-55-8 649544-58-1
649544-61-6 649544-65-0 649544-68-3 649544-71-8 649544-74-1
649544-79-6 649544-82-1 649544-85-4 649544-88-7 649544-91-2
649544-94-5 649544-97-8 649545-00-6 649545-03-9 649545-06-2
649545-09-5 649545-12-0 649545-15-3 649545-18-6 649545-21-1
649545-24-4 649545-27-7 649545-30-2 649545-33-5 649545-36-8
649545-39-1 649545-42-6 649545-45-9 649545-48-2 649545-51-7
649545-54-0 649545-57-3 649655-21-0 649655-22-1 649655-23-2

649655-24-3 649655-25-4 649655-26-5 649655-27-6 649655-28-7
649655-29-8 649655-30-1
RL: PRP (Properties)
(unclaimed sequence; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)

L3 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:696302 CAPLUS
DN 139:229237
TI Protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment
IN **Andersen, Peter**; Weldingh, Karin; Hansen, Christina Veggerby; Florio, Walter; Okkels, Li Mei Meng; Skjot, Rikke Louise Vinther; Rasmussen, Peter Birk
PA Den.
SO U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Ser. No. 60,428.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003165525	A1	20030904	US 2002-138473	20020502
	US 6641814	B1	20031104	US 1998-50739	19980330
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	US 2002094336	A1	20020718	US 2001-791171	20010220
PRAI	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-50739	A2	19980330		
	DK 1998-1281	A	19981008		
	US 2001-791171	B2	20010220		
	US 2002-60428	A2	20020129		
	EP 1998-913536	A3	19980401		

AB The present invention is based on the identification and characterization of 9 antigens, including Rv0652/CFP16, Rv2462c/TB51, Rv1984c/CFP21, Rv2185c/TB16, Rv1636/TB15A, Rv3451/CFP23, Rv3872/**RD1**-ORF3, Rv3354/CFP8A and Rv2623/TB32, from Mycobacterium **tuberculosis**. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, in an animal, including a human being. The invention related to treating **tuberculosis** using antigens isolated from Mycobacterium **tuberculosis**.

TI Protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment
IN **Andersen, Peter**; Weldingh, Karin; Hansen, Christina Veggerby; Florio, Walter; Okkels, Li Mei Meng; Skjot, Rikke Louise Vinther; Rasmussen, Peter Birk
AB The present invention is based on the identification and characterization of 9 antigens, including Rv0652/CFP16, Rv2462c/TB51, Rv1984c/CFP21, Rv2185c/TB16, Rv1636/TB15A, Rv3451/CFP23, Rv3872/**RD1**-ORF3, Rv3354/CFP8A and Rv2623/TB32, from Mycobacterium **tuberculosis**. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, in an animal, including a human being. The invention related to treating **tuberculosis** using antigens isolated from Mycobacterium **tuberculosis**.
ST Mycobacterium antigen sequence **tuberculosis** diagnosis treatment

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(Ag85A, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(Ag85B, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(Ag85C, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(CFP10, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ESAT-6, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(MPB59, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(MPB64, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(MPT32, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(MPT64, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**RD1**-ORF2, in fusion protein; protein and DNA sequences of

antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**RD1**-ORF5, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Rv0652/CFP16; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(Rv1036, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Rv1636/TB15A; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Rv1984c/CFP21; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Rv2185c/TB16; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Rv2462c/TB51; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Rv2623/TB32; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Rv3354/CFP8A; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study,

unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Rv3451/CFP23; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Rv3872/**RD1**-ORF3; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(TB10.4, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Diagnosis
(agents, **tuberculosis**; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Cell membrane
Cell wall
(antigen isolated from; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Fusion proteins (chimeric proteins)
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(antigens in; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Cytoplasm
(cytosol, antigen isolated from; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Animal
Human
(diagnosis of **tuberculosis** in; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Mycobacterium avium
Mycobacterium intracellulare
Mycobacterium marinum
Mycobacterium scrofulaceum
Mycobacterium szulgai
Mycobacterium xenopi
(expression of antigen CFP21 and CFP23 in; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Mycobacterium fortuitum
Mycobacterium kansasii
(expression of antigen CFP23 in; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Diagnosis
(immunodiagnosis; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Lipoproteins
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and

treatment)
IT Antibodies and Immunoglobulins
RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(monoclonal; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)
IT DNA sequences
Epitopes
Immunoassay
Molecular cloning
Mycobacterium **tuberculosis**
Protein sequences
Tuberculosis
Tuberculostatics
(protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)
IT Antibodies and Immunoglobulins
RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)
IT Gene, microbial
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)
IT Diagnosis
(serodiagnosis; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)
IT Mycobacterium africanum
Mycobacterium bovis
Mycobacterium **tuberculosis**
(**tuberculosis** caused by; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)
IT Mycobacterium
(virulent; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)
IT Crystallins
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(α-, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)
IT 592558-08-2P 592558-09-3P 592558-10-6P 592558-11-7P 592558-12-8P
592558-13-9P 592558-14-0P 592558-15-1P 592558-16-2P, Antigen T51 (Mycobacterium **tuberculosis**)
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)
IT 592557-99-8 592558-00-4 592558-01-5 592558-02-6 592558-03-7
592558-04-8 592558-05-9 592558-06-0 592558-07-1
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)
IT 592573-15-4 592573-16-5 592573-17-6 592573-18-7 592573-19-8
592573-20-1 592573-21-2 592573-22-3 592573-23-4 592573-24-5
592573-26-7 592573-27-8 592573-28-9 592573-29-0 592573-30-3
592573-31-4 592573-32-5 592573-33-6
RL: PRP (Properties)

(unclaimed nucleotide sequence; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT 592573-14-3 592573-25-6
RL: PRP (Properties)
(unclaimed protein sequence; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT 213992-11-1 213992-15-5 264285-55-4 264285-57-6 264285-59-8
RL: PRP (Properties)
(unclaimed sequence; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

L3 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:609858 CAPLUS
DN 139:163576
TI Mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of the **tuberculosis** complex
IN **Andersen, Peter**; Skjot, Rikke Louise Vinther
PA Den.
SO U.S. Pat. Appl. Publ., 135 pp., Cont.-in-part of U.S. Ser. No. 289,388, abandoned.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003147897	A1	20030807	US 2001-804980	20010313
	WO 9501441	A1	19950112	WO 1994-DK273	19940701
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, CZ, DE, DE, DK, DK, ES, FI, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, SK, TJ, TT, UA				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	EP 1508339	A1	20050223	EP 2004-77505	19940701
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI				
	US 5955077	A	19990921	US 1995-465640	19950605
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	US 2004013685	A1	20040122	US 2001-872505	20010601
PRAI	DK 1993-798	A	19930702		
	US 1993-123182	B2	19930920		
	WO 1994-DK273	A2	19940701		
	US 1995-465640	A1	19950605		
	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1999-289388	B2	19990412		
	EP 1994-919574	A3	19940701		
	EP 1998-913536	A3	19980401		
	US 1998-246191	B2	19981230		
	DK 1999-1020	A	19990713		
	US 1999-144011P	P	19990715		
	US 2000-615947	A2	20000713		
	WO 2000-DK398	A2	20000713		
	US 2001-804980	A2	20010313		

AB The present invention is based on the identification and characterization of a number of novel M. **tuberculosis** derived proteins and protein fragments, e.g. TB10.3 (ORF7-1 or Rv3019c), TB10.4 (CFP7 or Rv0288) and TB12.9 (ORF7-2 or Rv3017c), ESAT-6, MPT64, CFP10, **RD1**-ORF5,

RD1-ORF2, Rv1036, Ag85A, Ag85B, Ag85C, 19 kDa lipoprotein, MPT32, MPB59 and α-crystallin. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides.

TI Mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of the **tuberculosis** complex

IN **Andersen, Peter**; Skjot, Rikke Louise Vinther

AB The present invention is based on the identification and characterization of a number of novel M. **tuberculosis** derived proteins and protein fragments, e.g. TB10.3 (ORF7-1 or Rv3019c), TB10.4 (CFP7 or Rv0288) and TB12.9 (ORF7-2 or Rv3017c), ESAT-6, MPT64, CFP10, **RD1**-ORF5, **RD1**-ORF2, Rv1036, Ag85A, Ag85B, Ag85C, 19 kDa lipoprotein, MPT32, MPB59 and α-crystallin. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides.

ST Mycobacterium **tuberculosis** antigen gene antibody vaccine diagnosis skin test

575506-55-7 575506-56-8 575506-57-9 575506-58-0 575506-59-1
575506-60-4
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of the **tuberculosis** complex)

IT 575512-14-0 575512-20-8 575512-21-9 575512-22-0 575512-23-1
575512-24-2 575512-25-3 575512-26-4 575512-27-5 575512-28-6
575512-29-7 575512-30-0 575512-31-1 575512-32-2 575512-33-3
575512-34-4 575512-35-5 575512-36-6 575512-37-7 575512-38-8
575512-39-9 575512-40-2 575512-41-3 575512-43-5 575512-45-7
575512-47-9 575512-49-1 575512-51-5 575512-53-7 575512-55-9
575512-57-1 575512-59-3 575512-66-2 575512-67-3 575512-68-4
575512-69-5 575512-70-8 575512-71-9 575512-72-0 575512-73-1
575512-74-2 575512-75-3 575512-76-4 575512-77-5 575512-78-6
575512-79-7 575512-80-0 575512-81-1 575512-82-2 575512-83-3
575512-84-4 575512-85-5 575512-86-6 575512-87-7 575512-88-8
575512-89-9 575512-90-2 575512-91-3 575512-92-4 575512-93-5
575512-94-6 575512-95-7 575512-96-8 575512-97-9 575513-00-7
575513-01-8 575513-02-9 575513-03-0 575513-04-1 575513-05-2
575513-06-3 575513-07-4 575513-08-5 575513-10-9 575513-12-1
575513-14-3 575513-15-4 575513-16-5 575513-17-6 575513-18-7
575513-19-8 575513-20-1 575513-21-2 575513-22-3 575513-23-4
575513-24-5 575513-25-6 575513-26-7 575513-27-8 575513-32-5
575513-34-7 575513-36-9 575513-37-0 575513-39-2 575513-40-5
575513-41-6 575513-42-7 575513-43-8 575513-44-9 575513-45-0
RL: PRP (Properties)
(unclaimed nucleotide sequence; mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of the **tuberculosis** complex)

IT 575512-15-1 575512-16-2 575512-17-3 575512-18-4 575512-19-5
575512-42-4 575512-44-6 575512-46-8 575512-48-0 575512-50-4
575512-52-6 575512-54-8 575512-56-0 575512-58-2 575512-60-6
575512-61-7 575512-62-8 575512-63-9 575512-64-0 575512-65-1
575512-98-0 575512-99-1 575513-09-6 575513-11-0 575513-13-2
575513-29-0 575513-30-3 575513-31-4 575513-33-6 575513-35-8
575513-38-1
RL: PRP (Properties)
(unclaimed protein sequence; mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of the **tuberculosis** complex)

IT 213992-07-5 213992-08-6 213992-10-0 213992-11-1 213992-13-3
213992-14-4 213992-15-5 213992-16-6 213992-17-7 213992-18-8
213992-19-9 213992-20-2 213992-21-3 213992-23-5 213992-24-6
RL: PRP (Properties)
(unclaimed sequence; mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of

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SYSTEM LIMITS EXCEEDED

L3 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:684968 CAPLUS
DN 129:300060
TI Novel antigens of Mycobacterium ***tuberculosis culture filtrates and the genes encoding and their diagnostic and prophylactic use
IN **Andersen, Peter**; Nielsen, Rikke; Rosenkrands, Ida; Weldingh, Karin; Rasmussen, Peter Birk; Oettinger, Thomas; Florio, Walter
PA Statens Serum Institut, Den.
SO PCT Int. Appl., 264 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9844119	A1	19981008	WO 1998-DK132	19980401
	W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2285625	AA	19981008	CA 1998-2285625	19980401
	AU 9868204	A1	19981022	AU 1998-68204	19980401
	AU 740545	B2	20011108		
	EP 972045	A1	20000119	EP 1998-913536	19980401
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001515359	T2	20010918	JP 1998-541074	19980401
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	CA 2319380	AA	19990520	CA 1998-2319380	19981008
	WO 9924577	A1	19990520	WO 1998-DK438	19981008
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1029053	A1	20000823	EP 1998-947412	19981008
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	NZ 504951	A	20010629	NZ 1998-504951	19981008
	AU 750173	B2	20020711	AU 1998-94338	19981008
	EP 1484405	A1	20041208	EP 2004-77071	19981008
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PRAI	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	EP 1998-913536	A3	19980401		
	WO 1998-DK132	W	19980401		
	EP 1998-947412	A3	19981008		
	WO 1998-DK438	W	19981008		

AB Culture filtrate antigens of Mycobacterium **tuberculosis** are characterized and cDNAs encoding them are cloned. Some of the proteins

are antigenic and suitable for use in vaccines and in diagnosis of infections, e.g. skin tests. A fusion protein of two of these antigens is a superior immunogen compared to the unfused proteins. Individual antigens from culture filtrates were identified by T cell mapping using T cells from memory immune mice. Genes for individual antigens were then cloned by screening a λgt11 expression vector with monoclonal antibodies. Manufacture of individual antigens with hexahistidine affinity labels is described.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Novel antigens of Mycobacterium **tuberculosis** culture filtrates and the genes encoding and their diagnostic and prophylactic use

IN **Andersen, Peter**; Nielsen, Rikke; Rosenkrands, Ida; Weldingh, Karin; Rasmussen, Peter Birk; Oettinger, Thomas; Florio, Walter

AB Culture filtrate antigens of Mycobacterium **tuberculosis** are characterized and cDNAs encoding them are cloned. Some of the proteins are antigenic and suitable for use in vaccines and in diagnosis of infections, e.g. skin tests. A fusion protein of two of these antigens is a superior immunogen compared to the unfused proteins. Individual antigens from culture filtrates were identified by T cell mapping using T cells from memory immune mice. Genes for individual antigens were then cloned by screening a λgt11 expression vector with monoclonal antibodies. Manufacture of individual antigens with hexahistidine affinity labels is described.

ST Mycobacterium culture filtrate antigen gene; vaccine **tuberculosis** Mycobacterium antigen gene

IT Lipoproteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(19 kDa, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(85 complex, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Chaperonins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DnaK, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ESAT6, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Chaperonins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GroEL, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Chaperonins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GroES, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MPT51, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MPT59, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MPT64, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Antigens
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(culture filtrate antigens of Mycobacterium; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT **Tuberculosis**
(diagnosis, vaccines against and diagnosis of; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Escherichia
Mycobacterium
Mycobacterium BCG
Pseudomonas
Salmonella
(expression host for Mycobacterium **tuberculosis** antigen genes; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(for antigens of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Hemagglutinins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heparin-binding, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Antibodies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, to antigens of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Mycobacterium **tuberculosis**
(novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Molecular cloning
(of antigen genes of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Fusion proteins (chimeric proteins)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(of antigens of Mycobacterium **tuberculosis**,for vaccines; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Protein sequences
(of antigens of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT DNA sequences
(of genes for antigens of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors
(pRVN01,expression vector for antigen genes of Mycobacterium **tuberculosis** on; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors
(pRVN02,expression vector for antigen genes of Mycobacterium **tuberculosis** on; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors
(pTO87, gene for antigen of Mycobacterium **tuberculosis** on; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors
(pTO88, gene for antigen of Mycobacterium **tuberculosis** on; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors
(pTO89, gene for antigen of Mycobacterium **tuberculosis** on; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors
(pTO90, gene for antigen of Mycobacterium **tuberculosis** on; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors
(pTO91, gene for antigen of Mycobacterium **tuberculosis** on; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors
(pTO96, gene for antigen of Mycobacterium **tuberculosis** on; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors
(pTO98, gene for antigen of Mycobacterium **tuberculosis** on; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphate-binding, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(proline-rich, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**rd1**-orf2, for antigen of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture

filtrates and genes encoding and their diagnostic and prophylactic use)

IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**rd1**-orf3, for antigen of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**rd1**-orf4, for antigen of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**rd1**-orf5, for antigen of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**rd1**-orf8, for antigen of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**rd1**-orf9a, for antigen of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**rd1**-orf9b, for antigen of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Antibodies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(to antigens of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Mycobacterium africanum
Mycobacterium bovis
(**tuberculosis** caused by; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Diagnosis
(**tuberculosis**, vaccines against and diagnosis of; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Vaccines
(**tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT **Tuberculosis**
(vaccines against and diagnosis of; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Crystallins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α-, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT 213992-07-5 213992-08-6 213992-09-7D, amino acid-substituted analogs

213992-10-0 213992-11-1 213992-12-2 213992-13-3 213992-14-4
213992-15-5 213992-16-6 213992-17-7 213992-18-8 213992-19-9
213992-20-2 213992-21-3 213992-22-4 213992-23-5 213992-24-6
214072-43-2 214072-44-3 214072-45-4 214072-46-5 214072-47-6
214142-58-2
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(N-terminal peptide of Mycobacterium **tuberculosis** antigen; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT 151185-45-4, Protein (Mycobacterium BCG strain Tokyo ribosome)
208778-78-3 208782-67-6 208783-23-7 208783-90-8 208786-90-7
208788-06-1 208788-47-0 208790-41-4 208790-42-5 208853-48-9
208856-86-4 208857-49-2 208859-77-2 208863-45-0 208864-30-6
208865-40-1 208868-63-7 208871-19-6 208872-79-1 208874-21-9
208875-49-4 209053-74-7 210170-05-1 214348-60-4 214348-78-4
214348-84-2 214348-92-2 214349-12-9 214349-22-1 214349-24-3
214349-26-5 214349-38-9
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT 9002-13-5D, Urease, fusion products 9023-70-5D, Glutamine synthetase, fusion products 9029-06-5D, Alanine dehydrogenase, fusion products 9054-89-1D, Superoxide dismutase, fusion products
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as antigen of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT 214348-46-6 214348-59-1 214348-61-5 214348-62-6 214348-68-2
214348-69-3 214348-70-6 214348-76-2 214348-77-3 214348-79-5
214348-80-8 214348-81-9 214348-82-0 214348-83-1 214348-85-3
214348-86-4 214348-88-6 214348-89-7 214348-90-0 214348-91-1
214348-93-3 214349-11-8 214349-21-0 214349-23-2 214349-25-4
214349-28-7 214349-47-0 214349-53-8 214349-54-9 214349-57-2
214349-60-7 214349-62-9 214349-63-0
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

L3 ANSWER 12 OF 14 MEDLINE on STN
AN 2005184291 IN-PROCESS
DN PubMed ID: 15817755
TI Prospective evaluation of a whole-blood test using Mycobacterium **tuberculosis**-specific antigens ESAT-6 and CFP-10 for diagnosis of active **tuberculosis**.
AU Ravn Pernille; Munk Martin E; Andersen Ase B; Lundgren Bettina; Lundgren Jens D; Nielsen Lars N; Kok-Jensen Axel; **Andersen Peter**; Weldingh Karin
CS Department of Infectious Diseases, Hvidovre Hospital, Kettegards Alle 30, 2650 Hvidovre, Copenhagen, Denmark.. pravn@dadlnet.dk
SO Clinical and diagnostic laboratory immunology, (2005 Apr) 12 (4) 491-6. Journal code: 9421292. ISSN: 1071-412X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20050409
Last Updated on STN: 20050511
AB A new immunodiagnostic test based on the Mycobacterium **tuberculosis**-specific antigens CFP-10/ESAT-6(QFT-**RD1**) has been launched as an aid in the diagnosis of latent **tuberculosis** (TB) infection (LTBI). The aim of this study was to evaluate this test for the diagnosis of active TB. Eighty-two patients

with suspicion of TB and 39 healthy BCG-vaccinated persons were enrolled. Forty-eight had active TB, 25 did not, and 9 were excluded. Sensitivity and specificity of the test for active TB were evaluated in a prospective blinded manner in patients suspected of TB. The sensitivity of the QFT-**RD1** was 85% (40/48; confidence interval [CI], 75 to 96), and it was higher than the sensitivity of microscopy, 42% (20/48; CI, 27 to 56; P = 0.001), and culture, 59% (27/46; CI, 44 to 73; P = 0.009). Of patients with extrapulmonary TB, 92% (12/13) were QFT-**RD1** positive, whereas only 31% (4/13) were positive by microscopy and 42% (5/12) by culture ($P < 0.05$), and 87% (13/15) of those who were negative by both microscopy and culture were QFT-**RD1** positive. By combining microscopy and culture with the QFT-**RD1** test, sensitivity increased to 96% (CI, 90 to 102). Ten of 25 (40%) non-TB patients were QFT-**RD1** positive, resulting in a specificity of 60%. However, 80% (8/10) of these had risk-factors for TB, indicating latent infection in this group. In healthy controls, only 3% (1/39) were QFT-**RD1** positive. In conclusion, the QFT-**RD1** test is sensitive for diagnosis of TB, especially in patients with negative microscopy and culture. The accuracy of the QFT-**RD1** test will vary with the prevalence of LTBI. We suggest that the QFT-**RD1** test could be a very useful supplementary tool for the diagnosis of TB.

TI Prospective evaluation of a whole-blood test using Mycobacterium **tuberculosis**-specific antigens ESAT-6 and CFP-10 for diagnosis of active **tuberculosis**.

AU Ravn Pernille; Munk Martin E; Andersen Ase B; Lundgren Bettina; Lundgren Jens D; Nielsen Lars N; Kok-Jensen Axel; **Andersen Peter**; Weldingh Karin

AB A new immunodiagnostic test based on the Mycobacterium **tuberculosis**-specific antigens CFP-10/ESAT-6(QFT-**RD1**) has been launched as an aid in the diagnosis of latent **tuberculosis** (TB) infection (LTBI). The aim of this study was to evaluate this test for the diagnosis of active TB. Eighty-two. . . test for active TB were evaluated in a prospective blinded manner in patients suspected of TB. The sensitivity of the QFT-**RD1** was 85% (40/48; confidence interval [CI], 75 to 96), and it was higher than the sensitivity of microscopy, 42% (20/48;. . . 0.001), and culture, 59% (27/46; CI, 44 to 73; P = 0.009). Of patients with extrapulmonary TB, 92% (12/13) were QFT-**RD1** positive, whereas only 31% (4/13) were positive by microscopy and 42% (5/12) by culture ($P < 0.05$), and 87% (13/15) of those who were negative by both microscopy and culture were QFT-**RD1** positive. By combining microscopy and culture with the QFT-**RD1** test, sensitivity increased to 96% (CI, 90 to 102). Ten of 25 (40%) non-TB patients were QFT-**RD1** positive, resulting in a specificity of 60%. However, 80% (8/10) of these had risk-factors for TB, indicating latent infection in this group. In healthy controls, only 3% (1/39) were QFT-**RD1** positive. In conclusion, the QFT-**RD1** test is sensitive for diagnosis of TB, especially in patients with negative microscopy and culture. The accuracy of the QFT-**RD1** test will vary with the prevalence of LTBI. We suggest that the QFT-**RD1** test could be a very useful supplementary tool for the diagnosis of TB.

L3 ANSWER 13 OF 14 USPATFULL on STN
AN 2004:76186 USPATFULL
TI Therapeutic TB vaccine
IN **Andersen, Peter**, Bronshoj, DENMARK
Rosenkrands, Ida, Vaerlose, DENMARK
Stryhn, Anette, Virum, DENMARK
PI US 2004057963 A1 20040325
AI US 2003-617038 A1 20030711 (10)
PRAI DK 2002-1098 20020713
US 2002-401725P 20020807 (60)
DT Utility
FS APPLICATION
LREP HOWSON AND HOWSON, ONE SPRING HOUSE CORPORATION CENTER, BOX 457, 321 NORRISTOWN ROAD, SPRING HOUSE, PA, 19477
CLMN Number of Claims: 22
ECL Exemplary Claim: 1

DRWN 7 Drawing Page(s)
LN.CNT 6018
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Therapeutic vaccines comprising polypeptides expressed during the latent stage of mycobacteria infection are provided, as are multiphase vaccines, and methods for treating and preventing **tuberculosis**
.
IN **Andersen, Peter**, Bronshoj, DENMARK
AB . . . expressed during the latent stage of mycobacteria infection are provided, as are multiphase vaccines, and methods for treating and preventing **tuberculosis**.
SUMM [0002] The present invention discloses a therapeutic vaccine against latent or active **tuberculosis** infection caused by the **tuberculosis** complex microorganisms (Mycobacterium **tuberculosis**., M.bovis, M.africanum). The invention furthermore discloses a multi-phase vaccine that can be administered either prophylactically or therapeutically as well as a diagnostic reagent for the detection of latent stages of **tuberculosis**.
SUMM [0003] Human **tuberculosis** caused by Mycobacterium **tuberculosis** (M. **tuberculosis**) is a severe global health problem, responsible for approx. 3 million deaths annually, according to the WHO. The worldwide incidence of new **tuberculosis** (TB) cases had been falling during the 1960s and 1970s but during recent decades this trend has markedly changed in part due to the advent of AIDS and the appearance of multidrug resistant strains of M. **tuberculosis**.
SUMM [0004] Organisms of the **tuberculosis** complex can cause a variety of diseases, but the commonest route of invasion is by inhalation of bacteria. This initiates. . . for the rest of their life. Certainly, individuals who have been healthy for years or even decades can suddenly develop **tuberculosis**, which has proven to be caused by the same organism they were infected with many years previously. M. **tuberculosis** and other organisms of the TB complex are unique in that the mycobacteria can evade the immune response and survive. . .
SUMM [0005] The course of a M. **tuberculosis** infection runs essentially through 3 phases, as illustrated in FIG. 1. During the acute phase, the bacteria proliferate in the. . . a latent phase is established where the bacterial load is kept stable at a low level. In this phase M. **tuberculosis** goes from active multiplication to dormancy, essentially becoming non-replicating and remaining inside the granuloma. In some cases, the infection goes. . .
SUMM [0009] It has been suggested that the transition of M. **tuberculosis** from primary infection to latency is accompanied by changes in gene expression (see, for example, Honer zu Bentrup, 2001, which. . .
SUMM . . . candidate. The only way to determine if a protein is recognized by the immune system during latent infection with M. **tuberculosis** is to produce the given protein and test it in an appropriate assay as described herein. Of the more than. . .
DRWD . . . the infection. For analysis of therapeutic vaccinations a reactivation model is established, where aerosol infected mice are treated with anti-M **tuberculosis** drugs for 8 weeks from the peak of infection (6 weeks after infection). This induces a latent infection phase with. . .
DRWD . . . In FIG. 2A, the immunization was given as a prophylactic vaccine 6 weeks before the mice were given a M. **tuberculosis** infection (approx. 250 bacilli) through the aerosol route with. Bacterial numbers in the lung was enumerated 6 weeks post infection.. .
.
DETD [0024] The invention is related to preventing, treating and detecting infections caused by species of the **tuberculosis** complex (Mycobacterium **tuberculosis**, M. bovis, M. africanum) by the use of a polypeptide comprising a M. **tuberculosis** antigen or an immunogenic portion or other variant thereof, or by the use of a DNA sequence encoding a M. **tuberculosis** antigen or an immunogenic portion or other variant thereof. The invention discloses a new therapeutic vaccine against **tuberculosis** comprising antigens

induced during the latent stage of TB-infection. It also discloses a multiphase vaccine incorporating a combination of prophylactic and therapeutic antigens as well as diagnostic reagents for the detection of the latent stage of M. **tuberculosis** infection.

DETD . . . mycobacteria infection, which stage is characterized by low-oxygen tension in the microenvironment of the mycobacteria, for a therapeutic vaccine against **tuberculosis**.

DETD . . . with efficacy as prophylactic vaccines, where the fusion partner is selected from e.g. the group consisting of ESAT-6, TB10.4, CFP10, **RD1**-ORF5, **RD1**-ORF2, Rv1036, MPB64, MPT64, Ag85A, Ag85B (MPT59), MPB59, Ag85C, 19 kDa lipoprotein, MPT32.

DETD [0033] The invention further discloses a therapeutic vaccine against **tuberculosis** comprising one or more polypeptides or fragments hereof, which polypeptides are expressed during the latent stage of the mycobacteria infection,. . .

DETD [0036] The invention also discloses a method for treating an animal, including a human being, with **tuberculosis** caused by virulent mycobacteria, e.g., by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, comprising administering to the animal the above-mentioned vaccine.

DETD [0037] The invention also discloses a method for immunizing an animal, including a human being, against **tuberculosis** caused by virulent mycobacteria, e.g., by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, comprising administering to the animal the above mentioned vaccine.

DETD . . . to whom the vaccine has been administered, the amount of expressed antigen being effective to confer substantially increased resistance to **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, in an animal, including a human being.

DETD . . . use of a nucleic acid fragment according to the invention for the preparation of a composition for the diagnosis of **tuberculosis** caused by virulent mycobacteria, e.g., by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, and the use of a nucleic acid fragment according to the invention for the preparation of a pharmaceutical composition for the vaccination against **tuberculosis** caused by virulent mycobacteria, e.g., by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis.

DETD . . . a still further embodiment, the invention discloses a vaccine for immunizing an human being or other mammal or animal, against **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, comprising as the effective component a non-pathogenic microorganism, wherein at least one copy of a. . .

DETD [0049] (b) isolating the polypeptide from a whole mycobacterium, e.g. Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, from culture filtrate or from lysates or fractions thereof; or

DETD [0051] The invention also discloses a method of diagnosing **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, in an animal, including a human being, comprising intradermally injecting, in the animal, a polypeptide. . . immunogenic composition as defined above, a positive skin response at the location of injection being indicative of the animal having **tuberculosis**, and a negative skin response at the location of injection being indicative of the animal not having **tuberculosis** .

DETD [0052] In another embodiment, the invention discloses a method for immunizing an animal, including a human being, against **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, comprising administering to the animal the polypeptide as defined above, the immunogenic composition according to. . .

DETD . . . detecting binding of a antibody to said polypeptide, said binding being an indication that said subject is infected by

Mycobacterium **tuberculosis** or is susceptible to Mycobacterium **tuberculosis** infection.

DETD [0082] A preferred polypeptide within the present invention is an immunogenic antigen from M. **tuberculosis** produced when the organism is subjected to the stresses associated with latent infection. Such antigen can for example also be derived from the M. **tuberculosis** cell and/or M. **tuberculosis** culture filtrate. Thus, a polypeptide comprising an immunogenic portion of one of the above antigens may consist entirely of the immunogenic portion, or may contain additional sequences. The additional sequences may be derived from the native M. **tuberculosis** antigen or be heterologous and such sequences may, but need not, be immunogenic.

DETD . . . any other antigen with which it is natively associated, i.e. free of any other antigen from bacteria belonging to the **tuberculosis** complex or a virulent mycobacterium. This can be accomplished by preparing the polypeptide fragment by means of recombinant methods in. . .

DETD [0085] By the term "virulent mycobacterium" is understood a bacterium capable of causing the **tuberculosis** disease in an animal or in a human being. Examples of virulent mycobacteria include but are not limited to M. **tuberculosis**, M. africanum, and M. bovis. Examples of relevant animals are cattle, possums, badgers and kangaroos.

DETD [0088] By "a latently infected individual" is understood an individual, who has been infected by a virulent mycobacterium, e.g. M. **tuberculosis**, but shows no sign of active **tuberculosis** . It is likely that individuals who have been vaccinated, e.g. by BCG, or treated for TB may still retain the. . . for PPD reactivity. Nonetheless, in its most accurate sense, "latently-infected" may be used to describe any individual who has M. **tuberculosis** residing in their tissues but who is not clinically ill.

DETD [0101] In the context of providing candidate molecules for a new vaccine against **tuberculosis**, the subdominant epitopes are however as relevant as are the dominant epitopes since it has been shown (Olsen, 2000) that. . .

DETD . . . response may also be determined by the use of T cell lines derived from an immune individual or an M. **tuberculosis** -infected person where the T cell lines have been driven with either live mycobacteria, extracts from the bacterial cell or culture. . .

DETD [0114] In general, M. **tuberculosis** antigens, and DNA sequences encoding such antigens, may be prepared using any one of a variety of procedures.

DETD [0115] They may be purified as native proteins from the M. **tuberculosis** cell or culture filtrate by procedures such as those described above. Immunogenic antigens may also be produced recombinantly using a. . .

DETD . . . at least one fusion partner. The fusion partner can, in order to enhance immunogenicity, be another polypeptide derived from M. **tuberculosis**, such as of a polypeptide fragment derived from a bacterium belonging to the **tuberculosis** complex, such as ESAT-6, TB10.4, CFP10, **RD1**-ORF5, **RD1**-ORF2, Rv1036, MPB64, MPT64, Ag85A, Ag85B (MPT59), MPB59, Ag85C, 19 kDa lipoprotein, MPT32 and alpha-crystalline, or at least one T-cell epitope. . .

DETD . . . to the invention, and solubilizing or dispersing the polypeptide in a medium for a vaccine, and optionally adding other M. **tuberculosis** antigens and/or a carrier, vehicle and/or adjuvant substance.

DETD . . . from M. leprae. Antigens with therapeutic properties may be identified based on their ability to diminish the severity of M. **tuberculosis** infection in experimental animals or prevent reactivation of previous infection, when administered as a vaccine. The composition used for therapeutic. . .

DETD [0161] Cloning and Expression of Low Oxygen Induced M. **tuberculosis** Antigens in E. coli.

DETD [0162] A number of M **tuberculosis** genes are induced under low oxygen conditions. The upregulation of the genes listed in table 2 has been determined at. . .

DETD . . . Ammonium Sulfate, 0.2 mM of each of the four nucleotides, 0.2 μM of each primer and 10 ng of M. **tuberculosis** H37Rv

chromosomal DNA. The reaction mixtures were initially heated to 95° C. for 5 min., followed by 35 cycles of:. . .

DETD . . . with recombinant antigens. Six weeks after the last immunization, the mice are given an aerosol infection with approximately 250 M. **tuberculosis** bacilli. The protective capacity of the vaccine is evaluated by enumeration of the bacteria in spleen and lung 6 weeks. . .

DETD . . . reactivation model of latent TB has been established (van Pinxteren, 2000) (FIG. 1B). An aerosol infection with approximately 250 M. **tuberculosis** bacilli is given and at the peak of infection 6 weeks later, the mice receive an 8-week course of anti-mycobacterial. . .

DETD . . . cells is significantly higher in the unimmunized group. ESAT6 is an antigen produced in high amounts by the actively-growing M. **tuberculosis** bacteria. The level of the ESAT6 specific immune response in infected mice could therefore be indicative the degree of actively-growing. . . have in fact demonstrated such a correlation between the level of ESAT6 response and degree of disease in both M. **tuberculosis**-infected humans and M. bovis-infected cattle (Doherty, 2002, Vordermeier, 2002). Therefore, the higher ESAT6 response in the unimmunized group of latently-infected. . .

DETD . . . lungs of the Rv0569 vaccinated mice, whereas neither ESAT6 nor BCG are able to inhibit the growth of the M. **tuberculosis** bacteria when given as a vaccine during latent infection. That is, the induction of Rv0569 T cell responses can participate. . .

DETD [0182] Anon. 2001. Global **Tuberculosis** Control. WHO Report.

DETD [0202] Danish Patent application PA 2000 00666 "Nucleic acid fragments and polypeptide fragments derived from M. **tuberculosis**"

DETD [0203] Danish Patent application PA 1999 01020 (WO 01/23388) " **Tuberculosis** vaccine and diagnostic based on the Mycobacterium **tuberculosis** esat-6 gene family".

DETD [0204] Patent application U.S. Ser. No. 09/0505,739 "Nucleic acid fragments and polypeptide fragments derived from M. **tuberculosis** "

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 1
LENGTH: 273
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 1
Val Glu Pro Lys Arg Ser Arg Leu Val Val Cys Ala Pro Glu Pro Ser
1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 2
LENGTH: 152
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 2
Met Ser Pro Gly Ser Arg Arg Ala Ser Pro Gln Ser Ala Arg Glu Val
1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 3
LENGTH: 114
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 3
Val Glu Ser Glu Pro Leu Tyr Lys Leu Lys Ala Glu Phe Phe Lys Thr
1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 4
LENGTH: 344
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 4
Met Pro Ile Ala Thr Pro Glu Val Tyr Ala Glu Met Leu Gly Gln Ala
1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 5

LENGTH: 113
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 5
Met Gly Glu His Ala Ile Lys Arg His Met Arg Gln Arg Lys Pro Thr
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 6
LENGTH: 380
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 6
Val Ala Gly Asn Pro Asp Val Val Thr Val Leu Leu Gly Gly Asp Val
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 7
LENGTH: 397
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 7
Val Thr Asp His Val Arg Glu Ala Asp Asp Ala Asn Ile Asp Asp Leu
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 8
LENGTH: 446
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 8
Met Val Glu Pro Gly Asn Leu Ala Gly Ala Thr Gly Ala Glu Trp Ile
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 9
LENGTH: 210
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 9
Met Ile Ala Thr Thr Arg Asp Arg Glu Gly Ala Thr Met Ile Thr Phe
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 10
LENGTH: 80
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 10
Met Thr Asn Val Gly Asp Gln Gly Val Asp Ala Val Phe Gly Val Ile
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 11
LENGTH: 652
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 11
Val Thr Val Thr Pro Arg Thr Gly Ser Arg Ile Glu Glu Leu Leu Ala
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 12
LENGTH: 395
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 12
Met Arg Gly Gln Ala Ala Asn Leu Val Leu Ala Thr Trp Ile Ser Val
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 13
LENGTH: 94
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 13

Met Cys Gly Asp Gln Ser Asp His Val Leu Gln His Trp Thr Val Asp
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 14
LENGTH: 560
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 14
Met Ile Pro Thr Met Thr Ser Ala Gly Trp Ala Pro Gly Val Val Gln
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 15
LENGTH: 143
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 15
Met Ile Thr Asn Leu Arg Arg Arg Thr Ala Met Ala Ala Ala Gly Leu
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 16
LENGTH: 905
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 16
Leu Ser Ala Ser Val Ser Ala Thr Thr Ala His His Gly Leu Pro Ala
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 17
LENGTH: 258
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 17
Met Ser Phe His Asp Leu His His Gln Gly Val Pro Phe Val Leu Pro
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 18
LENGTH: 285
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 18
Val Val Lys Arg Ser Arg Ala Thr Arg Leu Ser Pro Ser Ile Trp Ser
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 19
LENGTH: 285
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 19
Val Val Lys Arg Ser Arg Ala Thr Arg Leu Ser Pro Ser Ile Trp Ser
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 20
LENGTH: 114
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 20
Val Thr Tyr Val Ile Gly Ser Glu Cys Val Asp Val Met Asp Lys Ser
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 21
LENGTH: 279
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 21
Met Asn Gln Ser His Lys Pro Pro Ser Ile Val Val Gly Ile Asp Gly
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 22

LENGTH: 339
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 22
Met Thr Glu Pro Ala Ala Trp Asp Glu Gly Lys Pro Arg Ile Ile Thr
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 23
LENGTH: 681
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 23
Val Leu Met Thr Ala Ala Ala Asp Val Thr Arg Arg Ser Pro Arg Arg
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 24
LENGTH: 144
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 24
Met Ala Thr Thr Leu Pro Val Gln Arg His Pro Arg Ser Leu Phe Pro
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 25
LENGTH: 331
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 25
Met Pro Asp Thr Met Val Thr Thr Asp Val Ile Lys Ser Ala Val Gln
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 26
LENGTH: 195
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 26
Met Pro Leu Leu Thr Ile Gly Asp Gln Phe Pro Ala Tyr Gln Leu Thr
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 27
LENGTH: 272
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 27
Met Ser Gly Arg Gly Glu Pro Thr Met Lys Thr Ile Ile Val Gly Ile
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 28
LENGTH: 393
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 28
Met Arg Asp Ala Ile Pro Leu Gly Arg Ile Ala Gly Phe Val Val Asn
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 29
LENGTH: 413
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 29
Met Ala Ser Ser Ala Ser Asp Gly Thr His Glu Arg Ser Ala Phe Arg
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 30
LENGTH: 120
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 30

Met Ser Thr Gln Arg Pro Arg His Ser Gly Ile Arg Ala Val Gly Pro
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 31
LENGTH: 374
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 31
Met Arg Ser Glu Arg Leu Arg Trp Leu Val Ala Ala Glu Gly Pro Phe
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 32
LENGTH: 179
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 32
Met Leu His Arg Asp Asp His Ile Asn Pro Pro Arg Pro Arg Gly Leu
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 33
LENGTH: 375
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 33
Val Thr Gln Thr Gly Lys Arg Gln Arg Arg Lys Phe Gly Arg Ile Arg
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 34
LENGTH: 371
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 34
Met Arg Val Gly Ile Pro Thr Glu Thr Lys Asn Asn Glu Phe Arg Val
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 35
LENGTH: 104
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 35
Met Val Ile Arg Phe Asp Gln Ile Gly Ser Leu Val Leu Ser Met Lys
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 36
LENGTH: 344
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 36
Val Leu Lys Asn Ala Val Leu Leu Ala Cys Arg Ala Pro Ser Val His
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 37
LENGTH: 336
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 37
Val Trp Ser Ala Ser Gly Gly Gln Cys Gly Lys Tyr Leu Ala Ala Ser
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 38
LENGTH: 110
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 38
Val Val Gln Gly Arg Thr Val Leu Phe Arg Thr Ala Glu Gly Ala Lys
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 39

LENGTH: 463
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 39
Met Asn His Leu Thr Thr Leu Asp Ala Gly Phe Leu Lys Ala Glu Asp
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 40
LENGTH: 332
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 40
Met Asn Thr His Phe Pro Asp Ala Glu Thr Val Arg Thr Val Leu Thr
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 41
LENGTH: 578
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 41
Met Thr Thr Gly Gly Leu Val Asp Glu Asn Asp Gly Ala Ala Met Arg
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 42
LENGTH: 268
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 42
Met Ser Asp Pro Arg Pro Ala Arg Ala Val Val Val Gly Ile Asp Gly
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 43
LENGTH: 181
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 43
Met Thr Glu Tyr Glu Gly Pro Lys Thr Lys Phe His Ala Leu Met Gln
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 44
LENGTH: 274
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 44
Met Thr Trp Ala Asp Glu Val Leu Ala Gly His Pro Phe Val Val Ala
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 45
LENGTH: 248
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 45
Val Ser Asp Gly Glu Gln Ala Lys Ser Arg Arg Arg Arg Gly Arg Arg
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 46
LENGTH: 819
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 46
gtggaaccga aacgcagtcg cctcgtcgta tgtgcacccg agccatcgca cgcgcgggaa 60
ttcccggatg tcgccgtatt ctccggcggc cgggctaacg catcccaggc cgaacggttg 120
gctcgtgccg tgggtcgcgt gttggccgat cggggcgtca ccgggggtgc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 47
LENGTH: 819
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 47
gtggaaccga aacgcagtcg cctcgtcgta tgtgcacccg agccatcgca cgcgcgggaa 60
ttcccggatg tcgccgtatt ctccggcggc cgggctaacg catcccaggc cgaacggttg 120
gctcgtgccg tgggtcgcgt gttggccgat cggggcgtca ccgggggtgc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 48
LENGTH: 342
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 48
gtggagtccg aaccgctgta caagctcaag gcggagttct tcaaaaccct tgcgcatccg 60
gcgcggatca ggattttgga gctgctggtc gagcgggacc gttcggtcgg tgagttgctg 120
tcctcggacg tcggcctgga gtcgtcgaac ctgtcccagc agctgggtgt. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 49
LENGTH: 1032
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 49
atgcctatcg caacgcccga ggtctacgcg gagatgctcg gtcaggccaa acaaaactcg 60
tacgctttcc cggctatcaa ctgcacctcc tcggaaaccg tcaacgccgc gatcaaaggt 120
ttcgccgacg ccggcagtga cggaatcatc cagttctcga ccggtggcgc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 50
LENGTH: 339
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 50
atgggtgagc acgccatcaa gcggcacatg cggcaacgga agcctacgaa gcatccccta 60
gcccagaaac ggggcgcgcg gattctggtc ttcaccgacg atccccgcag gagcgtcctc 120
atagtgcccg gttgccacct ggattccatg cgccgagaaa agaacgcgta. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 51
LENGTH: 1140
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 51
gtggctggca atcctgatgt ggtgacggtg ctgctgggcg gtgacgtcat gctcggccgt 60
ggcgtcgatc agatcctgcc tcatcccggc aaaccgcaat tgcgcgaacg gtatatgcgg 120
gatgcgaccg gctatgttcg cctggccgag cgggtgaacg ggcgcattcc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 52
LENGTH: 1191
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 52
gtgacagacc acgtgcgcga ggcggacgac gcgaacatcg acgatctgtt gggcgacctg 60
ggcggtaccg cgcgcgccga gcgtgcgaag cttgtcgagt ggttgctcga gcagggcatc 120
acccccgacg agattcgggc gaccaacccg ccgttgctgc tggccacccg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 53
LENGTH: 1338
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 53
atggtagagc ccggcaattt ggcaggcgcg accggcgccg aatggatcgg ccggccaccg 60
cacgaggaat tgcagcgcaa agtgcgcccg ctgctgccat ccgacgatcc gttctacttc 120
ccacctgccg gctaccagca tgccgtgccc ggaacggtgt tgcgctcgcg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 54
LENGTH: 630
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 54
atgatcgcca caacccgcga tcgtgaagga gccaccatga tcacgtttag gctgcgcttg 60
ccgtgccgga cgatactgcg ggtgttcagc cgcaatccgc tggtgcgtgg gacggatcga 120
ctcgaggcgg tcgtcatgct gctggccgtc acggtctcgc tgctgactat. . .
DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 55
LENGTH: 240
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 55
atgaccaacg tcggtgacca gggggttgac gcggtcttcg gggtgatcta cccacctcag 60
gtcgcgctgg tcagtttcgg caagccggca caacgagttt gcgccgtcga cggcgcgatc 120
cacgtcatga cgaccgtgct ggctacgctg cccgctgacc acggctgcag. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 56
LENGTH: 1956
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 56
gtgacggtga caccacggac cggcagccgc atcgaggagc tgcttgcacg cagcggccgg 60
ttcttcatcc cgggtgagat ctcggcggat ctgcgtaccg tgacccgccg cggcggccgc 120
gacggcgacg tgttctatcg agaccggtgg agccacgaca aggtggtccg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 57
LENGTH: 1185
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 57
atgagagggc aagcggccaa tctcgtgctg gccacctgga tctcggtggt caacttctgg 60
gcgtggaacc tgatcggccc gctgtcgacc agctacgcgc gtgacatgtc actgtccagc 120
gccgaggcgt cgctgctcgt cgccaccccg atcctggtgg gtgcccttgg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 58
LENGTH: 282
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 58
atgtgcggcg accagtcgga tcacgtgctg cagcactgga ccgtcgacat atcgatcgac 60
gaacacgaag gattgactcg ggcgaaggca cggctgcgtt ggcgggaaaa ggaattggtg 120
ggtgttggcc tggcaaggct caatccggcc gaccgcaacg tccccgagat. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 59
LENGTH: 1680
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 59
atgattccca cgatgacatc ggccggctgg gcaccagggg tggtgcagtt ccgcgaatac 60
caacggcgtt ggctgcgcgg cgatgtcctc gccggcctga ccgtggccgc ctatctgatc 120
ccgcaagcga tggcgtatgc gaccgtggcg ggcctaccgc cggcagccgg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 60
LENGTH: 429
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 60
atgatcacaa acctccgacg ccgaaccgcg atggcagccg ccggcctagg ggctgctctc 60
gggctgggca tcctgctggt tccgacggtg gacgcccatc tcgccaacgg ttcgatgtcg 120
gaagtcatga tgtcggaaat tgccgggttg cctatccctc cgattatcca. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 61
LENGTH: 2715
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 61
ttgtcggcgt cagtgtctgc cacgacggct catcatggct tgccagcaca tgaagtggtg 60
ctgctgctgg agagcgatcc atatcacggg ctgtccgacg gcgaggccgc ccaacgacta 120
gaacgcttcg ggcccaacac cttggcggtg gtaacgcgcg ctagcttgct. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 62
LENGTH: 774
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 62

atgagtttcc acgatcttca tcaccaaggt gttccgttcg tgttgcccaa cgcctgggat 60
gtgccgtcgg ccctggccta cctcgcggag ggcttcacgg ctatcggcac aaccagtttc 120
ggggtctcgt ccagcggcgg gcacccggac gggcaccgcg ccactcgcgg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 63
LENGTH: 855
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 63
gtggtcaagc gctctcgggc aacccgactt tcgccgagca tctggtccgg atgggaatca 60
cctcagtgtc ggtccattcg ggcgcgattg ctgctacccc ggggtcggtc gcggccgccg 120
aacgccgatt gttgctggaa tcagctcgcg gtgacgcctg acacccggat. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 64
LENGTH: 885
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 64
atgtctaaac cccgcaagca gcacggagtt gtcgtcgggg tagatggttc gctcgaatcg 60
gatgccgccg cctgttgggg tgccaccgat gcggcgatga ggaacattcc gctgaccgtg 120
gtccacgtgg tgaacgccga tgtagcgacg tggccgccga tgccgtatcc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 65
LENGTH: 342
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 65
gtgacctatg tgatcggtag tgagtgcgtg gatgtgatgg acaagtcctg tgtgcaggag 60
tgtccggtcg actgtatcta tgagggcgcc cgaatgctct acatcaaccc cgacgagtgc 120
gtggattgtg gtgcgtgcaa accggcctgc cgcgtcgagg cgatctactg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 66
LENGTH: 837
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 66
atgaaccaat cacacaaacc cccatcgatc gtcgtcggta ttgatggctc gaagccggcc 60
gtgcaagccg cactgtgggc ggtcgacgag gcagccagcc gtgacatccc gctgcgtctg 120
ctgtacgcga tcgaacccga cgatcccggg tacgccgcac acggcgcggc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 67
LENGTH: 1017
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 67
atgacggagc cagcggcgtg ggacgaaggc aagccgcgaa tcatcacttt gaccatgaac 60
cccgccttgg acatcacgac gagcgtcgac gtggtgcgcc cgaccgagaa aatgcgttgt 120
ggcgcacctc gctacgatcc cggcggcggc ggtatcaatg tcgcccgcat. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 68
LENGTH: 2043
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 68
gtgctgatga ccgcagcggc tgatgtcacc cggcgctcgc cgcggcgcgt gttccgtgac 60
cgccgcgagg ccggccgggt gctggcggaa ttactcgccg cctatcggga ccagccggac 120
gtgattgtgc tcggcttggc ccggggtggc ctcccggtcg catgggaggt. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 69
LENGTH: 432
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 69
atggccacca cccttcccgt tcagcgccac ccgcggtccc tcttccccga gttttctgag 60
ctgttcgcgg ccttcccgtc attcgccgga ctccggccca ccttcgacac ccggttgatg 120
cggctggaag acgagatgaa agaggggcgc tacgaggtac gcgcggagct. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 70

LENGTH: 993
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 70
atgccggaca ccatggtgac caccgatgtc atcaagagcg cggtgcagtt ggcctgccgc 60
gcaccgtcgc tccacaacag ccagccctgg cgctggatag ccgaggacca cacggttgcg 120
ctgttcctcg acaaggatcg ggtgctttac gcgaccgacc actccggccg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 71
LENGTH: 585
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 71
atgccactgc taaccattgg cgatcaattc cccgcctacc agctcaccgc tctcatcggc 60
ggtgacctgt ccaaggtcga cgccaagcag cccggcgact acttcaccac tatcaccagt 120
gacgaacacc caggcaagtg gcgggtggtg ttcttttggc cgaaagactt. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 72
LENGTH: 816
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 72
atgtctggga gaggagagcc gacgatgaaa acaatcattg ttggtatcga tggttcgcac 60
gcggcgatta cggccgcatt gtgggggttt gacgaggcca tcagccgagc ggtgccgctg 120
cgactggtct cagtgatcaa gccgacacat ccgtccccgg acgactacga. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 73
LENGTH: 1179
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 73
atgcgtgatg cgatcccgct tgggcggatc gccgggtttg tggtgaacgt ccactggagc 60
gtgttggtga tcctgtggtt gttcacctgg agtctggcga ccatgttgcc gggtaccgtc 120
ggaggctacc cggccgtggt ctattggctt ctcggcgcag gtggcgcggt. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 74
LENGTH: 1239
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 74
atggcaagtt ctgcgagcga cggcacccac gaacgctcgg cttttcgcct gagtccaccg 60
gtcttgagcg gcgccatggg accgttcatg cacaccggtc tgtacgtcgc tcaatcgtgg 120
cgcgactatc tgggtcaaca gcccgataaa ctgccgatcg cacggcccac. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 75
LENGTH: 360
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 75
atgtccacgc aacgaccgag gcactccggt attcgggctg ttggccccta cgcatgggcc 60
ggccgatgtg gtcggatagg caggtggggg gtgcaccagg aggcgatgat gaatctagcg 120
atatggcacc cgcgcaaggt gcaatccgcc accatctatc aggtgaccga. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 76
LENGTH: 1122
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 76
atgcgatcag aacgtctccg gtggctggta gccgcagaag gtccgttcgc ctcggtgtat 60
ttcgacgact cgcacgacac tcttgatgcc gtcgagcgcc gggaagcgac gtggcgcgat 120
gtccggaagc atctcgaaag ccgcgacgcg aagcaggagc tcatcgacag. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 77
LENGTH: 537
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 77
atgctgcacc gcgacgatca catcaatccg ccgcggcccc gcgggttgga tgttccttgc 60

gcccgcctac gagcgacaaa tcccctgcgc gccttggcgc gttgcgttca ggcgggcaag 120
ccgggcacca gttcagggca tcggtccgtg ccgcatacgg cggacttgcg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 78
LENGTH: 1125
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 78
gtgacgcaaa ccggcaagcg tcagagacgc aaattcggtc gcatccgaca gttcaactcc 60
ggccgctggc aagccagcta caccggcccc gacggccgcg tgtacatcgc ccccaaaacc 120
ttcaacgcca agatcgacgc cgaagcatgg ctcaccgacc gccgccgcga. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 79
LENGTH: 1113
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 79
atgcgcgtcg gtattccgac cgagaccaaa aacaacgaat tccgggtggc catcaccccg 60
gccggcgtcg cggaactaac ccgtcgtggc catgaggtgc tcatccaggc aggtgccgga 120
gagggctcgg ctatcaccga cgcggatttc aaggcggcag gcgcgcaact. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 80
LENGTH: 312
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 80
atggtcatcc ggtttgatca aatagggtca ttggtcctct caatgaaatc ccttgcgtca 60
ctgtcgtttc agcggtgtct gcgcgagaat tctagtttgg tcgcggcgct ggaccggctc 120
gatgctgcgg tcgatgagct gagcgctttg tcgtttgatg cgttgaccac. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 81
LENGTH: 1032
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 81
gtgctcaaga acgcagtctt gctggcatgc cgggcgccgt cggtgcacaa cagccagccc 60
tggcgttggg tggccgaaag cggctccgag cacactactg tgcacctgtt cgtcaaccgc 120
caccgaacgg tgccggccac cgaccattcc ggccggcaag cgatcatcag. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 82
LENGTH: 1011
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 82
gtgtggtccg cctcgggtgg gcagtgcggg aagtatcttg ccgcctcgat ggtgctgcag 60
cttgatgggt tggaacgtca cggtgtgttg gagtttgggc gtgaccgcta tggccccgag 120
gtgcgtgagg agctgttggc gatgagtgcg gccagcatcg atcgttatct. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 83
LENGTH: 330
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 83
gtggtgcaag gccgcaccgt gctgtttcgt accgcggagg gcgccaaatt attttcagcc 60
gtcgcgaagt gcgcggtggc tttcgaggcg gacgaccaca acgttgccga gggctggagc 120
gtgatcgtca aggttcgcgc ccaggtgctg acgaccgacg cgggggtccg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 84
LENGTH: 1389
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 84
atgaatcacc taacgacact tgacgccggg tttctcaagg cagaagacgt ggatcggcac 60
gtgagtctgg caatcggcgc tctggcggtc atcgaggggc cggctcccga tcaggaagcc 120
ttcttatcgt cgctcgctca acgcctacgt ccctgtaccc ggttcgggca. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 85
LENGTH: 996

TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 85
atgaacaccc atttcccgga cgccgaaacc gtgcgaacgg ttctcaccct ggccgtccgg 60
gccccctcca tccacaacac gcagccgtgg cggtggcggg tatgcccgac gagtctggag 120
ctgttctcta gacccgatat gcagctgcgt agcaccgatc cggacgggcg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 86
LENGTH: 1734
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 86
atgacaacag ggggcctcgt cgacgaaaac gacggcgccg caatgcgtcc actgcgtcac 60
acgctctccc aactacgcct gcacgagctg ctggtcgagg tgcaggaccg ggtcgagcag 120
atcgtcgagg gccgggaccg cctcgatggt ctggtggagg ccatgctcgt. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 87
LENGTH: 804
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 87
atgagcgatc ctcggccagc tcgggcagtg gtcgttggta tcgacgggtc aagggcggca 60
acgcatgcgg cgttgtgggc ggtcgatgag gcggtgaacc gagacattcc gctgcgactg 120
gtgtacgtca tcgatccgtc ccaactgtcc gccgccggcg agggcggtgg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 88
LENGTH: 543
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 88
atgacagaat acgaagggcc taagacaaaa ttccacgcgt taatgcagga acagattcat 60
aacgaattca cagcggcaca acaatatgtc gcgatcgcgg tttatttcga cagcgaagac 120
ctgccgcagt tggcgaagca tttttacagc caagcggtcg aggaacgaaa. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 89
LENGTH: 822
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 89
atgacatggg ccgacgaggt gctcgccgga catccctttg tggttgctca ccgtggtgcg 60
tcggcggctc ggccggagca tacccttgcc gcctacgacc tggcgctcaa agagggcgcc 120
gacggcgtgg aatgtgatgt gcggttgacc cgggacgggc atctggtctg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 90
LENGTH: 744
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 90
gtgtccgacg gcgaacaagc caaatcacgt cgacgccggg ggcggcgccg cgggcggcgc 60
gctgcggcta cagccgagaa tcacatggac gcccaaccgg ccggcgacgc caccccgacc 120
ccggcaacgg cgaagcggtc ccggtcccgc tcacctcgtc gcgggtcgac. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 91
LENGTH: 88
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 91
Met Lys Ala Lys Val Gly Asp Trp Leu Val Ile Lys Gly Ala Thr Ile
1 5 10. . .
CLM What is claimed is:
1. A method for inducing an immune response to latent **tuberculosis** in an individual, said method comprising the step of delivering a composition comprising one or more polypeptides or fragments thereof,. . .
2. The method according to claim 1, wherein said individual is infected by a virulent mycobacterium, e.g. M. **tuberculosis**, and is not vaccinated with BCG against **tuberculosis**.

6. A therapeutic vaccine against **tuberculosis** comprising one or more polypeptides or fragments hereof, which polypeptides are expressed during the latent stage of the mycobacteria infection,. . . . . vaccine according to claim 9 where the fusion partners is selected from the group consisting of ESAT-6, ESAT-6-Ag85B, TB10.4, CFP10, **RD1**-ORF5, **RD1**-ORF2, Rv1036, MPB64, MPT64, Ag85A, Ag85B (MPT59), MPB59, Ag85C, 19 kDa lipoprotein, MPT32.

. . . 13. A multiphase vaccine according to claim 12 where the antigen components with prophylactic activity comprises ESAT-6, ESAT-6-Ag85B, TB10.4, CFP10, **RD1**-ORF5, **RD1**-ORF2, Rv1036, MPB64, MPT64, Ag85A, Ag85B (MPT59), MPB59, Ag85C, 19 kDa lipoprotein or MPT32.

18. A method for treating an animal, including a human being, with **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, comprising administering to the animal the vaccine according to claim 6.

19. A method for immunizing an animal, including a human being, against **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, comprising administering to the animal the vaccine according to claim 12.

20. A method of diagnosing **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, in an animal, including a human being, comprising application or intradermally injecting, in the animal,. . . . encoding these polypeptides, a positive skin response at the location of injection or application being indicative of the animal having **tuberculosis**, and a negative skin response at the location of injection or application being indicative of the animal not having **tuberculosis**.

22. A method of diagnosing Mycobacterium **tuberculosis** infection in a subject comprising: (a) contacting a polypeptides or fragments hereof, which polypeptides are expressed during the latent stage. . . . detecting binding of an antibody to said polypeptide, said binding being an indication that said subject is infected by Mycobacterium **tuberculosis** or is susceptible to Mycobacterium **tuberculosis** infection.

L3 ANSWER 14 OF 14 USPATFULL on STN
AN 2002:178550 USPATFULL
TI Nucleic acid fragments and polypeptide fragments derived from M. **tuberculosis**
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PA STATENS SERUM INSTITUT (non-U.S. corporation)
PI US 2002094336 A1 20020718
AI US 2001-791171 A1 20010220 (9)
RLI Division of Ser. No. US 1998-50739, filed on 30 Mar 1998, PENDING
PRAI DK 1997-376 19970402
DK 1997-1277 19971110
US 1997-44624P 19970418 (60)
US 1998-70488P 19980105 (60)
DT Utility
FS APPLICATION
LREP FROMMER LAWRENCE & HAUG LLP, 745 FIFTH AVENUE, NEW YORK, NY, 10151
CLMN Number of Claims: 53
ECL Exemplary Claim: 1
DRWN 6 Drawing Page(s)

LN.CNT 6134
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is based on the identification and characterization of a number of M. **tuberculosis** derived novel proteins and protein fragments (SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171). The invention is directed to the polypeptides and immunologically active fragments thereof, the genes encoding them, immunological compositions such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, respectively.
TI Nucleic acid fragments and polypeptide fragments derived from M. **tuberculosis**
IN **Andersen, Peter**, Bronshoj, DENMARK
AB The present invention is based on the identification and characterization of a number of M. **tuberculosis** derived novel proteins and protein fragments (SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48,. . .
SUMM [0001] The present invention relates to a number of immunologically active, novel polypeptide fragments derived from the Mycobacterium **tuberculosis**, vaccines and other immunologic compositions containing the fragments as immunogenic components, and methods of production and use of the polypeptides. The invention also relates to novel nucleic acid fragments derived from M. **tuberculosis** which are useful in the preparation of the polypeptide fragments of the invention or in the diagnosis of infection with M. **tuberculosis** . The invention further relates to certain fusion polypeptides, notably fusions between ESAT-6 and MPT59.
SUMM [0002] Human **tuberculosis** (hereinafter designated "TB") caused by Mycobacterium **tuberculosis** is a severe global health problem responsible for approximately 3 million deaths annually, according to the WHO. The worldwide incidence. . . has markedly changed this trend due to the advent of AIDS and the appearance of multidrug resistant strains of M. **tuberculosis**.
SUMM [0005] Immunity to M. **tuberculosis** is characterized by three basic features; i) Living bacilli efficiently induces a protective immune response in contrast to killed preparations;. . .
SUMM [0006] Short term-culture filtrate (ST-CF) is a complex mixture of proteins released from M. **tuberculosis** during the first few days of growth in a liquid medium (Andersen et al., 1991). Culture filtrates has been suggested. . .
SUMM . . . invention is i.a. based on the identification and characterization of a number of previously uncharacterized culture filtrate antigens from M. **tuberculosis**. In animal models of TB, T cells mediating immunity are focused predominantly to antigens in the regions 6-12 and 17-30. . . the Sanger Database (cf. below) with the genes encoding CFP21 and CFP25, (cfp25 and cfp21respectively), shows homology to two M. **tuberculosis** DNA sequences, orf19A and orf23. The two sequences, orf19a and orf23, encode to putative proteins CFP19A and CFP23 with the. . .
SUMM [0011] The present invention is also based on the identification of a number of putative antigens from M. **tuberculosis** which are not present in Mycobacterium bovis BCG strains. The nucleotide sequences encoding these putative antigens are: **rd1**-orf2, **rd1** -orf3, **rd1**-orf4, **rd1**-orf5, **rd1**-orf5, **rd1**-orf9a, and **rd1**-orf9b.
SUMM . . . 58

CFP28	22		
CFP29	23	15	16
CFP30A	85	59	60
CFP30B	171	144	145
CFP50	86	61	62
MPT51		41	42
CWP32	77	152	153
RD1-ORF8		67	68
RD1-ORF2		71	72

RD1-ORF9B	69	70
RD1-ORF3	87	88
RD1-ORF9A	93	94
RD1-ORF4	89	90
RD2-ORF5	91	92
MPT59-ESAT6		172
ESAT6-MPT59		173

SUMM . . . in a) with respect to the ability of evoking a protective immune response against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex, or

SUMM . . . in a) with respect to the ability of evoking a protective immune response against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex,

SUMM . . . any other antigen with which it is natively associated, i.e. free of any other antigen from bacteria belonging to the **tuberculosis** complex. This can be accomplished by preparing the polypeptide fragment by means of recombinant methods in a non-mycobacterial host cell. . .

SUMM . . . and any one of 168-171 denotes any continuous stretch of at least 6 amino acid residues taken from the M. **tuberculosis** derived polypeptides in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, any one of 17-23, 42, 48,. . . being immunological equivalent thereto with respect to the ability of conferring increased resistance to infections with bacteria belonging to the **tuberculosis** complex. Thus, included is also a polypeptide from different sources, such as other bacteria or even from eukaryotic cells.

SUMM . . . in a guinea pig and/or in a primate such as a human being against infections with bacteria belonging to the **tuberculosis** complex which is at least 20% of the acquired increased resistance conferred by Mycobacterium bovis BCG and also at least. . . other organ homogenates isolated from the mouse or guinea pig receiving a challenge infection with a virulent strain of M. **tuberculosis**, or, in a primate such as a human being, being assessed by determining the protection against development of clinical **tuberculosis** in a vaccinated group versus that observed in a control group receiving a placebo or BCG (preferably the increased resistance. . .

SUMM . . . diagnostically significant immune response in a mammal indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex; this diagnostically significant immune response can be in the form of a delayed type hypersensitivity reaction which can e.g.. . .

SUMM . . . isolated from the experimental animal which have received a challenge infection with a virulent strain of mycobacteria belonging to the **tuberculosis** complex after previously having been immunized with the polypeptide, as compared to the mycobacterial counts in a control group of experimental animals infected with the same virulent strain, which experimental animals have not previously been immunized against **tuberculosis**. The comparison of the mycobacterial counts may also be carried out with mycobacterial counts from a group of experimental animals. . .

SUMM . . . the ability of the polypeptide fragment of the invention to confer increased resistance is to compare the incidence of clinical **tuberculosis** in two groups of individuals (e.g. humans or other primates) where one group receives a vaccine as described herein which. . .

SUMM [0033] The "**tuberculosis**-complex" has its usual meaning, i.e. the complex of mycobacteria causing TB which are Mycobacterium **tuberculosis**, Mycobacterium bovis, Mycobacterium bovis BCG, and Mycobacterium africanum.

SUMM . . . other short peptide sequences), whereas the product which can

be isolated from short-term culture filtrates from bacteria belonging to the **tuberculosis** complex are free of these sequences. Although it may in some applications be advantageous to produce these polypeptides recombinantly and. . .

SUMM . . . weeks of primary infection or within 4 days after the mouse has been rechallenge infected with mycobacteria belonging to the **tuberculosis** complex, the induction performed by the addition of the polypeptide to a suspension comprising about 200,000 spleen cells per ml,. . .

SUMM [0050] 3) induces an IFN-γ release from bovine PBMC derived from animals previously sensitized with mycobacteria belonging to the **tuberculosis** complex, said release being at least two times the release observed from bovine PBMC derived from animals not previously sensitized with mycobacteria belonging to the **tuberculosis** complex.

SUMM . . . as to allow for multiple expression of relevant epitopes), and an other polypeptide derived from a bacterium belonging to the **tuberculosis** complex, such as ESAT-6, MPB64, MPT64, and MPB59 or at least one T-cell epitope of any of these antigens. Other. . .

SUMM . . . first amino acid sequence including at least one stretch of amino acids constituting a S-cell epitope derived from the M. **tuberculosis** protein ESAT-6 or MPT59, and a second amino acid sequence including at least one T-cell epitope derived from a M. **tuberculosis** protein different from ESAT-6 (if the first stretch of amino acids are derived from ESAT-6) or MPT59 (if the first. . .

SUMM . . . one, wherein the at least one T-cell epitope included in the second amino acid sequence is derived from a M. **tuberculosis** polypeptide (the "parent" polypeptide) selected from the group consisting of a polypeptide fragment according to the present invention and described. . . detail above and in the examples, or the amino acid sequence could be derived from any one of the M. **tuberculosis** proteins DnaK, GroEL, urease, glutamine synthetase, the proline rich complex, L-alanine dehydrogenase, phosphate binding protein, Ag 85 complex, HBHA (heparin. . .

SUMM [0078] isolating the polypeptide from whole mycobacteria of the **tuberculosis** complex or from lysates or fractions thereof, e.g. cell wall containing fractions, or

SUMM . . . interesting are rapid-growing mycobacteria, e.g. M. smegmatis, as these bacteria have a high degree of resemblance with mycobacteria of the **tuberculosis** complex and therefore stand a good chance of reducing the need of performing post-translational modifications of the expression product.

SUMM . . . been administered, the amount of expressed antigen being effective to confer substantially increased resistance to infections with mycobacteria of the **tuberculosis** complex in an animal, including a human being.

SUMM . . . in an immune diagnostic agent due to their extracellular presence in culture media containing metabolizing virulent mycobacteria belonging to the **tuberculosis** complex, or because of their high homologies with such extracellular antigens, or because of their absence in M. bovis BCG.

SUMM . . . to the invention, and solubilizing or dispersing the polypeptide in a medium for a vaccine, and optionally adding other M. **tuberculosis** antigens and/or a carrier, vehicle and/or adjuvant substance.

SUMM . . . defined above, or some but not all of the peptides may be derived from a bacterium belonging to the M. **tuberculosis** complex. In the latter example the polypeptides not necessarily fulfilling the criteria set forth above for polypeptides may either act. . .

SUMM . . . which is a vaccine for immunizing an animal, including a human being, against TB caused by mycobacteria belonging to the **tuberculosis**-complex, comprising as the effective component a microorganism, wherein one or more copies of a DNA sequence encoding a polypeptide as. . .

SUMM [0116] The invention also relates to a method of diagnosing TB caused by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis in an animal, including a human being, comprising

intradermally injecting, in the animal, a polypeptide. . .

SUMM . . . pertains to a method for immunising an animal, including a human being, against TB caused by mycobacteria belonging to the **tuberculosis** complex, comprising administering to the animal the polypeptide of the invention, or a vaccine composition of the invention as described. . .

SUMM . . . gene in the mycobacterial genome has been demonstrated to have a very limited distribution in other mycobacterial strains that M. **tuberculosis**, e.g. esat-6 is absent in both BCG and the majority of mycobacterial species isolated from the environment, such as M.. . . the invention are especially well-suited for performing the diagnosis of on-going or previous infection with virulent mycobacterial strains of the **tuberculosis** complex, and it is contemplated that it will be possible to distinguish between 1) subjects (animal or human) which have. . .

SUMM . . . vitro method for diagnosing ongoing or previous sensitization in an animal or a human being with bacteria belonging to the **tuberculosis** complex, the method comprising providing a blood sample from the animal or human being, and contacting the sample from the. . .

DRWD [0128] FIG. 1: Long term memory immune mice are very efficiently protected towards an infection with M. **tuberculosis**. Mice were given a challenge of M. **tuberculosis** and spleens were isolated at different time points. Spleen lymphocytes were stimulated in vitro with ST-CF and the release of. . .

DRWD . . . directed to molecules from 6-12 and 17-38 kDa. Splenic T cells were isolated four days after the challenge with M. **tuberculosis** and stimulated in vitro with narrow molecular mass fractions of ST-CF. The release of IFN-γwas investigated

DRWD . . . MPB51 (Ohara et al., 1995) are underlined at position 780. The nucleotides given in italics are not present in M. **tuberculosis** H37Rv.

DETD [0135] A group of efficiently protected mice was generated by infecting 8-12 weeks old female C57Bl/6j mice with 5+10.sup.4 M. **tuberculosis** i.v. After 30 days of infection the mice were subjected to 60 days of antibiotic treatment with isoniazid and were. .

DETD . . . used this model to identify single antigens recognized by protective T cells. Memory immune mice were reinfected with 1+10.sup.6 M. **tuberculosis** i.v. and splenic lymphocytes were harvested at day 4-6 of reinfection, a time point where this population is highly reactive. . .

DETD [0140] The recombinant λgt11 M. **tuberculosis** DNA library constructed by R. Young (Young, R. A. et al. 1985) and obtained through the World Health Organization IMMTUB. . .

DETD . . . In order to obtain the nucleotide sequence of the gene encoding the pv-2 binding protein, the approximately 3 kb M. **tuberculosis** derived EcoRI--EcoRI fragment from AA242 was subcloned in the EcoRI site in the pBluescriptSK+(Stratagene) and used to transform E. coli. . .

DETD [0150] Similarly, to obtain the nucleotide sequence of the gene encoding the st-3 binding protein, the approximately 5 kb M. **tuberculosis** derived EcoRI--EcoRI fragment from AA226 was subcloned in the EcoRI site in the pBluescriptSK+(Stratagene) and used to transform E. coli. . .

DETD . . . sequence obtained on the insert from lambda phage AA226, a search of homology to the nucleotide sequence of the M. **tuberculosis** genome was performed in the Sanger database (Sanger Mycobacterium **tuberculosis** database):

DETD . . . in BCG are stable deletions and/or multiple mutations which do not readily revert. While physiological differences between BCG and M. **tuberculosis** and M. bovis has been noted, the attenuating mutations which arose during serial passage of the original BCG strain has. . . (Harboe et al., 1996), later 3 large deletions in BCG have been identified (Mahairas et al., 1996). The region named **RD1** includes the gene encoding ESAT-6 and an other (RD2) the gene encoding MPT64. Both antigens have been shown to have. . . has been shown to have properties as a vaccine candidate (cf. PCT/DK94/00273 and PCT/DK/00270). In order to find new M. **tuberculosis** specific diagnostic antigens as well as antigens for a new vaccine against TB,

the **RD1** region (17.499 bp) of M. **tuberculosis** H37Rv has been analyzed for Open Reading Frames (ORF). ORFs with a minimum length of 96 bp have been predicted. . . . have possible diagnostic and/or vaccine potential, as they are deleted from all known BCG strains. The predicted ORFs include ESAT-6 (**RD1**-ORF7) and CFP10 (**RD1**-ORF6) described previously (Srensen et al., 1995), as a positive control for the ability of the algorithm. In the present is. . .

DETD [0176] Seven open reading frames (ORF) from the 17,499 kb **RD1** region (Accession no. U34848) with possible diagnostic and vaccine potential have been identified and cloned.

DETD [0177] Identification of the ORF's **rd1**-orf2, **rd1**-orf3, **rd1**-orf4, **rd1**-orf5, **rd1**-orf2, **rd1**-orf9a, and **rd1**-orf9b.

DETD [0178] The nucleotide sequence of **rd1**-orf2 from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 71. The deduced amino acid sequence of RD1-ORF2 is set forth in. . .

DETD [0179] The nucleotide sequence of **rd1**-orf3 from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 87. The deduced amino acid sequence of **RD1**-ORF2 is set forth in SEQ ID NO: 88.

DETD [0180] The nucleotide sequence of **rd1**-orf4 from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 89. The deduced amino acid sequence of **RD1**-ORF2 is set forth in SEQ ID NO: 90.

DETD [0181] The nucleotide sequence of **rd1**-orf5 from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 91. The deduced amino acid sequence of **RD1**-ORF2 is set forth in SEQ ID NO: 92.

DETD [0182] The nucleotide sequence of **rd1**-orf8 from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 67. The deduced amino acid sequence of **RD1**-ORF2 is set forth in SEQ ID NO: 68.

DETD [0183] The nucleotide sequence of **rd1**-orf9a from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 93. The deduced amino acid sequence of **RD1**-ORF2 is set forth in SEQ ID NO: 94.

DETD [0184] The nucleotide sequence of **rd1**-orf9b from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 69. The deduced amino acid sequence of **RD1**-ORF2 is set forth in SEQ ID NO: 70.

DETD [0185] The DNA sequence **rd1**-orf2 (SEQ ID NO: 71) contained an open reading frame starting with an ATG codon at position 889-891 and ending with a termination codon (TAA) at position 2662-2664 (position numbers referring to the location in **RD1**). The deduced amino acid sequence (SEQ ID NO: 72) contains 591 residues corresponding to a molecular weight of 64,525.

DETD [0186] The DNA sequence **rd1**-orf3 (SEQ ID NO: 87) contained an open reading frame starting with an ATG codon at position 2807-2809 and ending with a termination codon (TAA) at position 3101-3103 (position numbers referring to the location in **RD1**). The deduced amino acid sequence (SEQ ID NO: 88) contains 98 residues corresponding to a molecular weight of 9,799.

DETD [0187] The DNA sequence **rd1**-orf4 (SEQ ID NO: 89) contained an open reading frame starting with a GTG codon at position 4014-4012 and ending with a termination codon (TAG) at position 3597-3595 (position numbers referring to the location in **RD1**). The deduced amino acid sequence (SEQ ID NO: 90) contains 139 residues corresponding to a molecular weight of 14,210.

DETD [0188] The DNA sequence **rd1**-orf5 (SEQ ID NO: 91) contained an open reading frame starting with a GTG codon at position 3128-3130 and ending with a termination codon (TGA) at position 4241-4243 (position numbers referring to the location in **RD1**). The deduced amino acid sequence (SEQ ID NO: 92) contains 371 residues corresponding to a molecular weight of 37,647.

DETD [0189] The DNA sequence **rd1**-orf8 (SEQ ID NO: 67) contained an open reading frame starting with a GTG codon at position 5502-5500 and ending with a termination codon (TAG) at position 5084-5082 (position numbers referring to the location in **RD1**), and the deduced amino acid sequence (SEQ ID NO: 68) contains 139 residues with a molecular weight of 11,737.

DETD [0190] The DNA sequence **rd1**-orf9a (SEQ ID NO: 93) contained an open reading frame starting with a GTG codon at position 6146-6148 and ending with a termination codon (TAA) at position 7070-7072 (position

numbers referring to the location in **RD1**). The deduced amino acid sequence (SEQ ID NO: 94) contains 308 residues corresponding to a molecular weight of 33,453.

DETD [0191] The DNA sequence **rd1**-orf9b (SEQ ID NO: 69) contained an open reading frame starting with an ATG codon at position 5072-5074 and ending with a termination codon (TAA) at position 7070-7072 (position numbers referring to the location in **RD1**). The deduced amino acid sequence (SEQ ID NO: 70) contains 666 residues corresponding to a molecular weight of 70,650.

DETD [0192] Cloning of the ORF's **rd1**-orf2, **rd1**-orf3, **rd1**-orf4, **rd1**-orf5, **rd1**-orf8, **rd1**-orf9a, and **rd1**-orf9b.

DETD [0193] The ORF's **rd1**-orf2, **rd1**-orf3, **rd1**-orf4, **rd1**-orf5, **rd1**-orf8, **rd1**-orf9a and **rd1**-orf9b were PCR cloned in the pMST24 (Theisen et al., 1995) (**rd1**-orf3) or the pQE32 (QIAGEN) (**rd1**-orf2, **rd1**-orf4, **rd1**-orf5, **rd1**-orf8, **rd1**-orf9a and **rd1**-orf9b) expression vector. Preparation of oligonucleotides and PCR amplification of the **rd1**-orf encoding genes, was carried out as described in example 2. Chromosomal DNA from M. **tuberculosis** H37Rv was used as template in the PCR reactions. Oligonucleotides were synthesized on the basis of the nucleotide sequence from the **RD1** region (Accession no. U34848). The oligonucleotide primers were engineered to include an restriction enzyme site at the 5' end and. . .

DETD [0194] **rd1**-orf2.

DETD [0195] A BamHI site was engineered immediately 5' of the first codon of **rd1**-orf2, and a HindIII site was incorporated right after the stop codon at the 3' end. The gene **rd1**-orf2 was subcloned in pQE32, giving pTO96.

DETD [0196] **rd1**-orf3.

DETD [0197] A SmaI site was engineered immediately 5' of the first codon of **rd1**-orf3, and a NcoI site was incorporated right after the stop codon at the 3' end. The gene **rd1**-orf3 was subcloned in pMST24, giving pTO87.

DETD [0198] **rd1**-orf34.

DETD [0199] A BamHI site was engineered immediately 5' of the first codon of **rd1**-orf4, and a HindIII site was incorporated right after the stop codon at the 3' end. The gene **rd1**-orf4 was subcloned in pQE32, giving pTO89.

DETD [0200] **rd1**-orf5.

DETD [0201] A BamHI site was engineered immediately 5' of the first codon of **rd1**-orf5, and a HindIII site was incorporated right after the stop codon at the 3' end. The gene **rd1**-orf5 was subcloned in pQE32, giving pTO88.

DETD [0202] **rd1**-orf8.

DETD [0203] A BamHI site was engineered immediately 5' of the first codon of **rd1**-orf8, and a NcoI site was incorporated right after the stop codon at the 3' end. The gene **rd1**-orf8 was subcloned in pMST24, giving pTO98.

DETD [0204] **rd1**-orf9a.

DETD [0205] A BamHI site was engineered immediately 5' of the first codon of **rd1**-orf9a, and a HindIII site was incorporated right after the stop codon at the 3' end. The gene **rd1**-orf9a was subcloned in pQE32, giving pTO91.

DETD [0206] **rd1**-orf9b.

DETD [0207] A ScaI site was engineered immediately 5' of the first codon of **rd1**-orf9b, and a Hind III site was incorporated right after the stop codon at the 3' end. The gene **rd1**-orf9b was subcloned in pQE32, giving pTO90.

DETD [0209] Purification of recombinant **RD1**-ORF2, **RD1**-ORF3, **RD1**-ORF4, **RD1**-ORF5, **RD1**-ORF8, **RD1**-ORF9a and **RD1**-ORF9b.

DETD . . . the His-rRD1-ORF's were pooled and subsequently dialysed extensively against 25 mM Hepes, pH 8.0 before use.

TABLE 2

Sequence of the **rd1**-orf's oligonucleotides.sup.a.
Orientation and
oligonucleotide Sequences (5' → 3')
Position (nt)

Sense

PD1-ORF2f	CTGGGGATCCGCATGACTGCTGAACCG	886-903
PD1-ORF3f	CTTCCCGGGATGGAAAAAATGTCAC	
2807-2822		
RD1-ORF4f	GTAGGATCCTAGGAGACATCAGCGGC	
4028-4015		
RD1-ORF5f	CTGGGGATCCGCGTGATCACCATGCTGTGG	
3028-3045		
RD1-ORF8f	CTCGGATCCTGTGGGTGCAGGTCCGGCGATGGGC	
5502-5479		
RD1-ORF9af	GTGATGTGAGCTCAGGTGAAGAAGGTGAAG	
6144-6160		
RD1-ORFF9bf	GTGATGTGAGCTCCTATGGCGGCCGACTACGAC	
5072-5089		

Antisense

PD1-ORF2r	TGCAAGCTTTTAACCGGCGCTTGGGGGTGC	
2664-2644		
RD1-ORF3r	GATGCCATGGTTAGGCGAAGACGCCGGC	
3103-3086		
RD1-ORF4r	CGATCTAAGCTTGGCAATGGAGGTCTA	
3582-3597		
RD1-ORF5r	TGCAAGCTTTCACCAGTCGTCCTCTTCGTC	
4243-4223		
RD1-ORF8r	CTCCCATGGCTACGACAAGCTCTTCCGGCCGC	
5083-5105		
PDI-ORF9a/br	CGATCTAAGCTTTCAACGACGTCCAGCC	
7073-7056		

.sup.aThe oligonucleotides were constructed from the Accession number U34484 nucleotide sequence (Mahairas et al., 1996). Nucleotides (nt). . .

DETD [0211] The nucleotide sequences of **rd1**-orf2, **rd1**-orf3, **rd1**-orf4, **rd1**-orf5, **rd1**-orf8, **rd1**-orf9a, and **rd1**-orf9b from M. **tuberculosis** H37Rv are set forth in SEQ ID NO: 71, 87, 89, 91, 67, 93, and 69, respectively. The deduced amino acid sequences of **rd1**-orf2, **rd1**-orf3, **rd1**-orf4 **rd1**-orf5, **rd1**-orf8, **rd1**-orf9a, and **rd1**-orf9b are set forth in SEQ ID NO: 72, 88, 90, 92, 68, 94, and 70, respectively.

DETD . . . the Linocin M18 protein from Brevibacterium linens, a set of degenerated primers were constructed for PCR cloning of the M. **tuberculosis** gene encoding CFP29. PCR reactions were containing 10 ng of M. **tuberculosis** chromosomal DNA in 1+low salt Taq+ buffer from Stratagene supplemented with 250 μM of each of the four nucleotides (Boehringer. . .

DETD . . . first 150 bp of this sequence was used for a homology search using the Blast program of the Sanger Mycobacterium **tuberculosis** database:

DETD [0230] (http//www.sanger.ac.uk/projects/M-**tuberculosis**/blast_server).

DETD [0231] This program identified a Mycobacterium **tuberculosis** sequence on cosmid cy444 in the database that is nearly 100% identical to the 150 bp sequence of the CFP29. . .

DETD . . . sequence from each of the proteins were used for a homology search using the blast program of the Sanger Mycobacterium **tuberculosis** database:

DETD . . . protein purified from culture filtrate starts at amino acid 8 and therefore the length of the protein occurring in M. **tuberculosis** culture filtrate is 175 amino acids. This gives a theoretical molecular weigh at 18517 Da and a pI at 6.8.. . .

DETD . . . with gene specific primers, for recombinant expression in E. coli of the proteins. PCR reactions contained 10 ng of M. **tuberculosis** chromosomal DNA in 1+low salt Taq+ buffer from Stratagene supplemented with 250 mM of each of the four nucleotides

(Boehringer. . .

DETD . . . sequence from each of the proteins was used for a homology search using the blast program of the Sanger Mycobacterium **tuberculosis** database:

DETD [0296] http: //www.sanger.ac.uk/projects/m-**tuberculosis** /TB-blast-server.

DETD . . . were found in the Sanger database. This could be due to the fact that only approximately 70% of the M. **tuberculosis** genome had been sequenced when the searches were performed. The genes encoding these proteins could be contained in the remaining. . .

DETD . . . CFP25, EXAMPLE 3) belong to a family of fungal cutinase homologs. Among the most homologous sequences were also two Mycobacterium **tuberculosis** sequences found on cosmid MTCY13E12. The first, MTCY13E12.04 has 46% and 50% identity to CFP25 and CFP21 respectively. The second,. . .

DETD [0336] CFP25A: CFP25A has 95% identity in a 241 aa overlap to a putative M. **tuberculosis** thymidylate synthase 450 aa accession No p28176).

DETD [0343] PCR reactions contained 10 ng of M. **tuberculosis** chromosomal DNA in 1+ low salt Taq+ buffer from Stratagene supplemented with 250 mM of each of the four nucleotides. . .

DETD . . . sequence from each of the proteins was used for a homology search using the blast program of the Sanger Mycobacterium **tuberculosis** genome database:

DETD [0366] http//www.sanger.ac.uk/projects/m-**tuberculosis** /TB-blast-server.

DETD [0374] PCR reactions contained 10 ng of M. **tuberculosis** chromosomal DNA in 1+ low salt Taq+ buffer from Stratagene supplemented with 250 mM of each of the four nucleotides. . .

DETD . . . were used for the preparation and handling of DNA (Sambrook et al., 1989). The gene mpt51 was cloned from M. **tuberculosis** H37Rv chromosomal DNA by the use of the polymerase chain reactions (PCR) technology as described previously (Oettinger and Andersen, 1994).. .

.

DETD [0392] The nucleotide sequence of the cloned 952 bp M. **tuberculosis** H37Rv PCR fragment, pTO52, containing the Shine Dalgarno sequence, the signal peptide sequence and the structural gene of MPT51, and. . .

DETD . . . the N-terminal region of the mature protein at position 144. Therefore, a structural gene encoding MPT51, mpt51, derived from M. **tuberculosis** H37Rv was found to be located at position 144-945 of the sequence shown in FIG. 5. The nucleotide sequence of. . .

DETD . . . compared to the strong recognition of the antigen that has been found during the recall of memory immunity to M. **tuberculosis**. ESAT-6 has been found in ST-CF in a truncated version were amino acids 1-15 have been deleted. The deletion includes. . .

DETD [0415] PCR reactions contained 10 ng of M. **tuberculosis** chromosomal DNA in 1+ low salt Taq+ buffer from Stratagene supplemented with 250 mM of each of the four nucleotides. . .

DETD . . . same high level as ST-CF.

TABLE 5

IFN-γ release from splenic memory effector cells from C57BL/6J mice isolated after reinfection with M. **tuberculosis** after stimulation with native antigens.

Antigen.sup.a	IFN-γ (pg/ml).sup.b
ST-CF	12564
CFP7	ND.sup.d
CFP9	ND
CFP17	9251
CFP20	2388
CFP21	10732. . .

DETD [0432] The skin test activity of the purified proteins was tested in M. **tuberculosis** infected guinea pigs.

DETD [0433] 1 group of guinea pigs was infected via an ear vein with

1+10.sup.4 CFU of M. **tuberculosis** H37Rv in 0,2 ml PBS. After 4 weeks skin tests were performed and 24 hours after injection erythema diameter was. . .

DETD . . . significant Delayed Type Hypersensitivity (DTH) reaction.

TABLE 6

DTH erythema diameter in guinea pigs infected with 1 + 10.sup.4 CFU of M. **tuberculosis**, after stimulation with native antigens.

Antigen.sup.a	Skin reaction (mm).sup.b
Control	2.00
PPD.sup.c	15.40 (0.53)
CFP7	ND.sup.e
CFP9	ND
CFP17	11.25. . .

DETD . . . animal models.

TABLE 6a

DTH erythema diameter of recombinant antigens in outbred guinea pigs infected with 1 + 10.sup.4 CFU of M. **Tuberculosis**.

Antigen.sup.a	Skin reaction (mm).sup.b	
Control	2.9	(0.3)
PPD.sup.a	14.5	(1.0)
CFP 7a	13.6	(1.4)
CFP 17	6.8	(1.9)
CFP 20. . .		

DETD . . . and A.SW(H-2.sup.s) mice (Bomholtegaard, Ry) were given intravenous infections via the lateral tail vein with an inoculum of 5+10.sup.4 M. **tuberculosis** suspended in PBS in a vol. of 0.1 ml. 14 days postinfection the animals were sacrificed and spleen cells were. . .

DETD . . . female C57BL/6j(H-2.sup.b) mice (Bomholtegaard, Ry) were given intravenous infections via the lateral tail vein with an inoculum of 5+10.sup.4 M. **tuberculosis** suspended in PBS in a vol. of 0.1 ml. After 1 month of infection the mice were treated with isoniazid.

. .	++	+++	+	
rCFP29	+++	+++	+++	++
rMPT51	+	-	-	-

Mouse IFN-γ release during recall of memory immunity to M. **tuberculosis**.

-: no response;
+: 1/3 of ST-CF;
++: 2/3 of ST-CF;
+++: level of ST-CF.

DETD . . . +++

rCFP21	+++
rCFP22	-
rCFP29	+
rCFP25	+++
rMPT51	+

Mouse IFN-γ release 14 days after primary infection with M. **tuberculosis**.

-: no response;
+: 1/3 of ST-CF;
++: 2/3 of ST-CF;
+++: level of ST-CF.

DETD . . . donors with no known exposure to patients with TB and from patients with culture or microscopy proven infection with Mycobacterium **tuberculosis**. Blood samples were drawn from the TB patients 1-4 months after diagnosis.

DETD [0472] 6 weeks after the last immunization the mice were aerosol challenged with 5+10.sup.6 viable Mycobacterium **tuberculosis** /ml. After 6 weeks of infection the mice were

killed and the number of viable bacteria in lung and spleen. . .

DETD [0476] Species distribution of cfp7, cfp9, mpt51, **rd1**-orf2, **rd1**-orf3, **rd1**-orf4, **rd1**-orf5, **rd1**-orf8, **rd1**-orf9a and **rd1**-orf9b as well as of cfp7a, cfp7b, cfp10a, cfpl7, cfp21, cfp21, cfp22, cfp22a, cfp23, cfp25 and cfp25a.

DETD [0477] Presence of cfg7, cfp9, mpt51, **rd1**-orf2, **rd1**-orf3, **rd1**-orf4, **rd1**-orf5, **rd1**-orf8, **rd1**-orf9a and **rd1**-orf9b in different mycobacterial species.

DETD [0478] In order to determine the distribution of the cfp7, cfp9, mpt51, **rd1**-orf2, **rd1**-orf3, **rd1**-orf4, **rd1**-orf5, **rd1**-orf8, **rd1**-orf9a and **rd1**-orf9b genes in species belonging to the M. **tuberculosis**-complex and in other mycobacteria PCR and/or Southern blotting was used. The bacterial strains used are listed in TABLE 10. Genomic. . .

DETD . . . were used in order to determine the distribution of the cfp7, cfp9 and mpt51 gene in species belonging to the **tuberculosis** -complex and in other mycobacteria. The bacterial strains used are listed in TABLE 10. PCR was performed on genomic DNA prepared. . .

DETD . . . bp). cfp9: stR3 and stF1 (351 bp).

TABLE 10

Mycobacterial strains used in this Example.

	Species and strain(s)		Source
1.	M. **tuberculosis**	H 3 7 R vATCC.sup.a (ATCC 27294)	
2.		H 3 7 R aATCC (ATCC 25177)	
3.		Erdman	Obtained from A.

. . .

DETD . . . plc, Little Chalfont, United Kingdom) with a vacuum transfer device (Milliblot, TM-v; Millipore Corp., Bedford, Mass.). The cfp7, cfp9, mpt51, **rd1**-orf2, **rd1**-orf3, **rd1**-orf4, **rd1**-orf5, **rd1**-orf8, **rd1**-orf9a and **rd1**-orf9b gene fragments were amplified by PCR from the plasmids pRVN01, pRVN02, pT052, pT087, pT088, pT089, pT090, pT091, pT096 or pT098. . .

DETD [0487] cfp7, cfp9 and mpt51 were found in the M. **tuberculosis** coinplex including BCG and the environmental mycobacteria; M. avium, M. kansasii, M. marinum, M. intracellular and M. flavescens. cfp9 was. .

DETD [0489] There is a strong band at around 26 kDa in M. **tuberculosis** H37Rv, Ra, Erdman, M. bovis AN5, M. bovis BCG substrain Danish 1331 and M. africanum. No band was seen in the region in any other tested mycobacterial strains.

TABLE 13a

Interspecies analysis of the **rd1**-orf2, **rd1**-orf3, **rd1**-orf4, **rd1**-orf5, **rd1**-orf8, **rd1**-orf9a and **rd1**-orf9b genes by Southern blotting.

	Species and strain	**rd1**-orf2	**rd1**-orf3	**rd1**-orf4	**rd1**-orf5	**rd1**-orf8	**rd1**-orf9a	**rd1**-orf9b
1.	M. tub. H37Rv	+	+	+	+	+	+	+
2.	M. bovis	+	+	+	+	N.D.	+	+
3.	M..							

. .

DETD [0490] Positive results for **rd1**-orf2, **rd1**-orf3, **rd1**-orf4, **rd1**-orf5, **rd1**-orf8, **rd1**-orf9a and **rd1**-orf9b were only obtained when using genomic DNA

from M. **tuberculosis** and M. bovis, and not from M. bovis BCG or other mycobacteria analyzed except **rd1**-orf4 which also was found in M. marinum.

DETD [0492] Southern blotting was carried out as described for **rd1**-orf2, **rd1**-orf3, **rd1**-orf4, **rd1**-orf5, **rd1**-orf8, **rd1**-orf9a and **rd1**-orf9b. The cfp7a, cfp7b, cfploa, cfp17, cfp20, cfp21, cfp22, cfp22a, cfp23, cfp25 and cfp25a gene fragments were amplified by PCR from. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 1
LENGTH: 381
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 1
ggccgccggt acctatgtgg ccgccgatgc tgcggacgcg tcgacctata ccgggttctg 60
atcgaaccct gctgaccgag aggacttgtg atgtcgcaaa tcatgtacaa ctaccccgcg 120
atgttgggtc acgccgggga tatggccgga tatgccggca cgctgcagag. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 2
LENGTH: 96
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 2
Met Ser Gln Ile Met Tyr Asn Tyr Pro Ala Met Leu Gly His Ala Gly
1 5. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 3
LENGTH: 467
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 3
gggtagccgg accacggctg ggcaaagatg tgcaggccgc catcaaggcg gtcaaggccg 60
gcgacggcgt cataaacccg gacggcacct tgttggcggg ccccgcggtg ctgacgcccg 120
acgagtacaa ctcccggctg gtggccgccg acccggagtc caccgcggcg. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 4
LENGTH: 108
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 4
Met Ala Ala Asp Pro Glu Ser Thr Ala Ala Leu Pro Asp Gly Ala Gly
1 5. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 5
LENGTH: 889
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 5
cgggtctgca cggatccggg ccgggcaggg caatcgagcc tgggatccgc tggggtgcgc 60
acatcgcgga cccgtgcgcg gtacggtcga gacagcggca cgagaaagta gtaagggcga 120
taataggcgg taaagagtag cgggaagccg gccgaacgac tcggtcagac. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 6
LENGTH: 162
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 6
Met Thr Asp Met Asn Pro Asp Ile Glu Lys Asp Gln Thr Ser Asp Glu
1 5. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 7
LENGTH: 898
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 7
tcgactccgg cgccaccggg caggatcacg gtgtcgacgg ggtcgccggg gaatcccacg 60
ataaccactc ttcgcgccat gaatgccagt gttggccagg cgctggcctg gcgtccacgc 120
cacacaccgc acagattagg acacgccggc ggcgcagccc tgcccgaaag. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 8
LENGTH: 165
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 8
Met Ala Gln Ile Thr Leu Arg Gly Asn Ala Ile Asn Thr Val Gly Glu
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 9
LENGTH: 1054
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 9
ataatcagct caccgttggg accgacctcg accaggggtc ctttgtgact gccgggcttg 60
acgcggacga ccacagagtc ggtcatcgcc taaggctacc gttctgacct ggggctgcgt 120
gggcgccgac gacgtgaggc acgtcatgtc tcagcggccc accgccacct. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 10
LENGTH: 217
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 10
Met Thr Pro Arg Ser Leu Val Arg Ile Val Gly Val Val Val Ala Thr
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 11
LENGTH: 949
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 11
agccgctcgc gtggggtcaa ccgggtttcc acctgctcac tcattttgcc gcctttctgt 60
gtccgggccg aggcttgcgc tcaataactc ggtcaagttc cttcacagac tgccatcact 120
ggcccgtcgg cgggctcgtt gcgggtgcgc cgcgtgcggg tttgtgttcc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 12
LENGTH: 182
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 12
Met Ala Asp Cys Asp Ser Val Thr Asn Ser Pro Leu Ala Thr Ala Thr
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 13
LENGTH: 1060
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 13
tggaccttca ccggcggtcc cttcgcttcg ggggcgacac ctaacatact ggtcgtcaac 60
ctaccgcgac accgctggga ctttgtgcca ttgccggcca ctcggggccg ctgcggcctg 120
gaaaaattgg tcgggcacgg gcggccgcgg gtcgctacca tcccactgtg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 14
LENGTH: 219
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 14
Met Gly Ala Ala Ala Ala Met Leu Ala Ala Val Leu Leu Leu Thr Pro
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 15
LENGTH: 1198
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 15
cagatgctgc gcaacatgtt tctcggcgat ccggcaggca acaccgatcg agtgcttgac 60
ttttccaccg cggtgaccgg cggactgttc ttctcaccca ccatcgactt tctcgaccat 120
ccaccgcccc taccgcaggc ggcgacgcca actctggcag ccgggtcgct. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 16
LENGTH: 265
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 16
Met Asn Asn Leu Tyr Arg Asp Leu Ala Pro Val Thr Glu Ala Ala Trp
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 17
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: VARIANT
LOCATION: (1)
OTHER INFORMATION: Ala is Ala or Ser
SEQUENCE: 17
Ala Glu Leu Asp Ala Pro Ala Gln Ala Gly Thr. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 18
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 18
Ala Gln Ile Thr Leu Arg Gly Asn Ala Ile Asn Thr Val Gly Glu
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 19
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: UNSURE
LOCATION: (3)
OTHER INFORMATION: Xaa is unknown
SEQUENCE: 19
Asp Pro Xaa Ser Asp Ile Ala Val Val Phe Ala Arg Gly. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 20
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 20
Thr Asn Ser Pro Leu Ala Thr Ala Thr Ala Thr Leu His Thr Asn
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 21
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: UNSURE
LOCATION: (2)
OTHER INFORMATION: Xaa is unknown
SEQUENCE: 21
Ala Xaa Pro Asp Ala Glu Val Val Phe Ala Arg Gly Arg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 22
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: UNSURE
LOCATION: (1)
OTHER INFORMATION: Xaa is unknown
SEQUENCE: 22
Xaa Ile Gln Lys Ser Leu Glu Leu Ile Val Val Thr Ala. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 23
LENGTH: 19
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 23
Met Asn Asn Leu Tyr Arg Asp Leu Ala Pro Val Thr Glu Ala Ala Trp
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 24
LENGTH: 34
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 24
cccggctcga gaacctstac cgcgacctsg cscc 34
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 25
LENGTH: 37
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 25
gggccggatc cgasgcsgcg tccttsacsg gytgcca 37
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 26
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 26
ggaagcccca tatgaacaat ctctaccg 28
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 27
LENGTH: 32
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 27
cgcgctcagc ccttagtgac tgagcgcgac cg 32
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 28
LENGTH: 24
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 28
ctcgaattcg ccgggtgcac acag 24
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 29
LENGTH: 25
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 29
ctcgaattcg cccccatacg agaac 25
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 30
LENGTH: 15
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 30
gtgtatctgc tggac 15
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 31
LENGTH: 15
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 31
ccgactggct ggccg 15
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 32
LENGTH: 24
TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 32
gaggaattcg cttagcggat cgca 24
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 33
LENGTH: 15
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 33
cccacattcc gttgg 15
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 34
LENGTH: 15
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 34
gtccagcaga tacac 15
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 35
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 35
gtacgagaat tcatgtcgca aatcatg 27
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 36
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 36
gtacgagaat tcgagcttgg ggtgccg 27
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 37
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 37
cgattccaag cttgtggccg ccgacccg 28
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 38
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 38
cgttagggat cctcatcgcc atggtgttgg 30
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 39
LENGTH: 26
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 39
cgttagggat ccggttccac tgtgcc 26
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 40
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 40
cgttagggat cctcaggtct tttcgatg 28
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 41
LENGTH: 952
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 41
gaattcgccg ggtgcacaca gccttacacg acggaggtgg acacatgaag ggtcggtcgg 60
cgctgctgcg ggcgctctgg attgccgcac tgtcattcgg gttgggcggt gtcgcggtag 120
ccgcggaacc caccgccaag gccgccccat acgagaacct gatggtgccg. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 42
LENGTH: 299
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 42
Met Lys Gly Arg Ser Ala Leu Leu Arg Ala Leu Trp Ile Ala Ala Leu
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 43
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 43
gcaacacccg ggatgtcgca aatcatg 27
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 44
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 44
gtaacacccg gggtggccgc cgacccg 27
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 45
LENGTH: 37
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 45
ctactaagct tggatcccta gccgccccat ttggcgg 37
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 46
LENGTH: 38
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 46
ctactaagct tccatggtca ggtcttttcg atgcttac 38
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 47
LENGTH: 450
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 47
gtgccgcgct ccccagggtt cttatggttc gatatacctg agtttgatgg aagtccgatg 60
accagcagtc agcatacggc atggccgaaa agagtggggt gatgatggcc gaggatgttc 120
gcgccgagat cgtggccagc gttctcgaag tcgttgtcaa cgaaggcgat. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 48
LENGTH: 71
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 48
Met Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 49
LENGTH: 750
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 49
gggtacccat cgatgggttg cggttcggca ccgaggtgct aacgcacttg ctgacacact 60
gctagtcgaa aacgaggcta gtcgcaacgt cgatcacacg agaggactga ccatgacaac 120
ttcacccgac ccgtatgccg cgctgcccaa gctgccgtcc ttcagcctga. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 50
LENGTH: 176
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 50

Met Thr Thr Ser Pro Asp Pro Tyr Ala Ala Leu Pro Lys Leu Pro Ser
1 5. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 51
LENGTH: 800
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 51
tcatgaggtt catcggggtg atcccacgcc cgcagccgca ttcgggccgc tggcgagccg 60
gtgccgcacg ccgcctcacc agcctggtgg ccgccgcctt tgcggcggcc acactgttgc 120
ttacccccgc gctggcacca ccggcatcgg cgggctgccc ggatgccgag. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 52
LENGTH: 226
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 52
Met Ile Pro Arg Pro Gln Pro His Ser Gly Arg Trp Arg Ala Gly Ala
1 5. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 53
LENGTH: 700
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 53
ctaggaaagc ctttcctgag taagtattgc cttcgttgca taccgccctt tacctgcgtt 60
aatctgcatt ttatgacaga atacgaaggg cctaagacaa aattccacgc gttaatgcag 120
gaacagattc ataacgaatt cacagcggca caacaatatg tcgcgatcgc. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 54
LENGTH: 181
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 54
Met Thr Glu Tyr Glu Gly Pro Lys Thr Lys Phe His Ala Leu Met Gln
1 5. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 55
LENGTH: 950
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 55
tgggctcggc actggctctc ccacggtggc gcgctgattt ctccccacgg taggcgttgc 60
gacgcatgtt cttcaccgtc tatccacagc taccgacatt tgctccggct ggatcgcggg 120
taaaattccg tcgtgaacaa tcgacccatc cgcctgctga catccggcag. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 56
LENGTH: 262
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 56
Met Asn Asn Arg Pro Ile Arg Leu Leu Thr Ser Gly Arg Ala Gly Leu
1 5. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 57
LENGTH: 1000
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 57
cgaggagacc gacgatctgc tcgacgaaat cgacgacgtc ctcgaggaga acgccgagga 60
cttcgtccgc gcatacgtcc aaaagggcgg acagtgacct ggccgttgcc cgatcgcctg 120
tccattaatt cactctctgg aacacccgct gtagacctat cttctttcac. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 58
LENGTH: 291
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 58

Met Thr Trp Pro Leu Pro Asp Arg Leu Ser Ile Asn Ser Leu Ser Gly
1 5. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 59
LENGTH: 900
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 59
ttggcccgcg cgatcatcga aagccgttcg ggtgcggata ctttcggctc cgatggcggt 60
gagaagtgag ttttccgtat ttcatctcgc ctgagcaggc gatgcgcgag cgcagcgagt 120
tggcgcgtaa gggcattgcg cgggccaaaa gcgtggtggc gctggcctat. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 60
LENGTH: 248
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 60
Met Ser Phe Pro Tyr Phe Ile Ser Pro Glu Gln Ala Met Arg Glu Arg
1 5. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 61
LENGTH: 1560
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 61
gagtcattgc ctggtcggcg tcattccgta ctagtcggtt gtcggacttg acctactggg 60
tcaggccgac gagcactcga ccattagggt aggggccgtg acccactatg acgtcgtcgt 120
tctcggagcc ggtcccggcg ggtatgtcgc ggcgattcgc gccgcacagc. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 62
LENGTH: 464
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 62
Met Thr His Tyr Asp Val Val Val Leu Gly Ala Gly Pro Gly Gly Tyr
1 5. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 63
LENGTH: 550
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 63
ggcccggctc gcggccgccc tgcaggaaaa gaaggcctgc ccaggcccag actcagccga 60
gtagtcaccc agtaccccac accaggaagg accgcccatc atggcaaagc tctccaccga 120
cgaactgctg gacgcgttca aggaaatgac cctgttggag ctctccgact. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 64
LENGTH: 130
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 64
Met Ala Lys Leu Ser Thr Asp Glu Leu Leu Asp Ala Phe Lys Glu Met
1 5. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 65
LENGTH: 900
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 65
tgaacgccat cgggtccaac gaacgcagcg ctacctgatc accaccgggt ctgttagggc 60
tcttccccag gtcgtacagt cgggccatgg ccattgaggt ttcggtgttg cgggttttca 120
ccgattcaga cgggaatttc ggtaatccgc tgggggtgat caacgccagc. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 66
LENGTH: 228
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 66

Met Ala Ile Glu Val Ser Val Leu Arg Val Phe Thr Asp Ser Asp Gly
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 67
LENGTH: 500
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 67
gtttgtggtg tcggtggtct ggggggcgcc aactgggatt cggttggggt gggtgcaggt 60
ccggcgatgg gcatcggagg tgtgggtggt ttgggtgggg ccggttcggg tccggcgatg 120
ggcatggggg gtgtgggtgg tttgggtggg gccggttcgg gtccggcgat. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 68
LENGTH: 139
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 68
Met Gly Ala Gly Pro Ala Met Gly Ile Gly Gly Val Gly Gly Leu Gly
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 69
LENGTH: 2050
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 69
agcgcactct gagaggttgt catggcggcc gactacgaca agctcttccg gccgcacgaa 60
ggtatggaag ctccggacga tatggcagcg cagccgttct tcgaccccag tgcttcgttt 120
ccgccggcgc ccgcatcggc aaacctaccg aagcccaacg gccagactcc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 70
LENGTH: 666
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 70
Met Ala Ala Asp Tyr Asp Lys Leu Phe Arg Pro His Glu Gly Met Glu
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 71
LENGTH: 1890
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 71
gcagcgatga ggaggagcgg cgccaacggc ccgcgccggc gacgatgcaa agcgcagcga 60
tgaggaggag cggcgcgcat gactgctgaa ccggaagtac ggacgctgcg cgaggttgtg 120
ctggaccagc tcggcactgc tgaatcgcgt gcgtacaaga tgtggctgcc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 72
LENGTH: 591
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 72
Met Thr Ala Glu Pro Glu Val Arg Thr Leu Arg Glu Val Val Leu Asp
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 73
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 73
Asp Pro Val Asp Asp Ala Phe Ile Ala Lys Leu Asn Thr Ala Gly
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 74
LENGTH: 14
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: UNSURE

LOCATION: (14)
OTHER INFORMATION: Xaa is unknown
SEQUENCE: 74
Asp Pro Val Asp Ala Ile Ile Asn Leu Asp Asn Tyr Gly. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 75
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: UNSURE
LOCATION: (5)
OTHER INFORMATION: Xaa is unknown
SEQUENCE: 75
Ala Glu Met Lys Xaa Phe Lys Asn Ala Ile Val Gln Glu. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 76
LENGTH: 14
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: VARIANT
LOCATION: (3)
OTHER INFORMATION: Ala is Ala or Gln
SEQUENCE: 76
Val Ile Ala Gly Met Val Thr His Ile His Xaa. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 77
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 77
Thr Asn Ile Val Val Leu Ile Lys Gln Val Pro Asp Thr Trp Ser
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 78
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 78
Ala Ile Glu Val Ser Val Leu Arg Val Phe Thr Asp Ser Asp Gly
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 79
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 79
Ala Lys Leu Ser Thr Asp Glu Leu Leu Asp Ala Phe Lys Glu Met
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 80
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: VARIANT
LOCATION: (4)
OTHER INFORMATION: Asp is Asp or Glu
SEQUENCE: 80
Asp Pro Ala Asp Ala Pro Asp Val Pro Thr Ala. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 81
LENGTH: 50
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 81
Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val

1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 82
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 82
Thr Thr Ser Pro Asp Pro Tyr Ala Ala Leu Pro Lys Leu Pro Ser
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 83
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 83
Thr Glu Tyr Glu Gly Pro Lys Thr Lys Phe His Ala Leu Met Gln
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 84
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 84
Thr Thr Ile Val Ala Leu Lys Tyr Pro Gly Gly Val Val Met Ala
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 85
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: UNSURE
LOCATION: (10)
OTHER INFORMATION: Xaa is unknown
SEQUENCE: 85
Ser Phe Pro Tyr Phe Ile Ser Pro Glu Xaa Ala Met Arg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 86
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 86
Thr His Tyr Asp Val Val Val Leu Gly Ala Gly Pro Gly Gly Tyr
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 87
LENGTH: 450
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 87
agcccggtaa tcgagttcgg gcaatgctga ccatcgggtt tgtttccggc tataaccgaa 60
cggtttgtgt acgggataca aatacaggga gggaagaagt aggcaaatgg aaaaaatgtc 120
acatgatccg atcgctgccg acattggcac gcaagtgagc gacaacgctc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 88
LENGTH: 98
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 88
Met Glu Lys Met Ser His Asp Pro Ile Ala Ala Asp Ile Gly Thr Gln
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 89
LENGTH: 460
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 89
gcaaccggct tttcgatcag ctgagacatc agcggcgtgc gggtcaacga cccacctgcg 60

ccaggtagcg actccgcgcg cagcaggccc gcgcccgcgc tggggcctga tccaccagcc 120
agcggatggt tcgacagcgg actggtgccg agcaggccca tctgcgcggc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 90
LENGTH: 139
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 90
Met Arg Val Asn Asp Pro Pro Ala Pro Gly Ser Asp Ser Ala Arg Ser
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 91
LENGTH: 1200
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 91
taataggccc ccaacacatc ggagggagtg atcaccatgc tgtggcacgc aatgccaccg 60
gagctaaata ccgcacggct gatggccggc gcgggtccgg ctccaatgct tgcggcggcc 120
gcgggatggc agacgctttc ggcggctctg gacgctcagg ccgtcgagtt. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 92
LENGTH: 371
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 92
Met Ile Thr Met Leu Trp His Ala Met Pro Pro Glu Leu Asn Thr Ala
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 93
LENGTH: 1000
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 93
gacgcgacac agaaatcctt aaggccggcg gccaaggggc cgaaggtgaa gaaggtgaag 60
ccccagaaac cgaaggccac gaagccgccc aaagtggtgt cgcagcgcgg ctggcgacat 120
tgggtgcatg cgttgacgcg aatcaacctg ggcctgtcac ccgacgagaa. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 94
LENGTH: 308
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 94
Met Lys Lys Val Lys Pro Gln Lys Pro Lys Ala Thr Lys Pro Pro Lys
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 95
LENGTH: 34
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 95
aagagtagat ctatgatggc cgaggatgtt cgcg 34
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 96
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 96
cggcgacgac ggatcctacc gcgtcgg 27
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 97
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 97
ccttgggaga tctttggacc ccggttgc 28
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 98
LENGTH: 25

TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 98
gacgagatct tatgggctta ctgac 25
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 99
LENGTH: 33
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 99
ccccccagat ctgcaccacc ggcatcggcg ggc 33
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 100
LENGTH: 24
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 100
gcggcggatc cgttgcttag ccgg 24
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 101
LENGTH: 32
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 101
ccggctgaga tctatgacag aatacgaagg gc 32
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 102
LENGTH: 24
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 102
ccccgccagg gaactagagg cggc 24
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 103
LENGTH: 38
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 103
ctgccgagat ctaccaccat tgtcgcgctg aaataccc 38
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 104
LENGTH: 25
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 104
cgccatggcc ttacgcgcca actcg 25
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 105
LENGTH: 32
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 105
ggcggagatc tgtgagtttt ccgtatttca tc 32
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 106
LENGTH: 25
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 106
cgcgtcgagc catggttagg cgcag 25
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 107
LENGTH: 32
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 107
gaggaagatc tatgacaact tcacccgacc cg 32
DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 108
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 108
catgaagcca tggcccgcag gctgcatg 28
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 109
LENGTH: 33
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 109
ggccgagatc tgtgacccac tatgacgtcg tcg 33
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 110
LENGTH: 36
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 110
ggcgcccatg gtcagaaatt gatcatgtgg ccaacc 36
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 111
LENGTH: 33
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 111
ccgggagatc tatggcaaag ctctccaccg acg 33
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 112
LENGTH: 32
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 112
cgctgggcag agctacttga cggtgacggt gg 32
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 113
LENGTH: 36
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 113
ggcccagatc tatggccatt gaggtttcgg tgttgc 36
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 114
LENGTH: 26
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 114
cgccgtgttg catggcagcg ctgagc 26
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 115
LENGTH: 24
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 115
ggacgttcaa gcgacacatc gccg 24
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 116
LENGTH: 24
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 116
cagcacgaac gcgccgtcga tggc 24
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 117
LENGTH: 26
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 117

acagatctgt gacggacatg aacccg 26
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 118
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 118
ttttccatgg tcacgggccc ccggtact 28
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 119
LENGTH: 26
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 119
acagatctgt gcccatggca cagata 26
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 120
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 120
tttaagcttc taggcgccca gcgcggc 27
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 121
LENGTH: 26
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 121
acagatctgc gcatgcggat ccgtgt 26
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 122
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 122
ttttccatgg tcatccggcg tgatcgag 28
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 123
LENGTH: 26
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 123
acagatctgt aatggcagac tgtgat 26
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 124
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 124
ttttccatgg tcaggagatg gtgatcga 28
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 125
LENGTH: 26
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 125
acagatctgc cggctacccc ggtgcc 26
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 126
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 126
ttttccatgg ctattgcagc tttccggc 28
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 127
LENGTH: 50
TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 127
Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val
1 5 . . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 128
LENGTH: 49
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 128
Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val
1 5 . . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 129
LENGTH: 50
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 129
Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val
1 5 . . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 130
LENGTH: 33
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 130
ccgggagatc tatggcaaag ctctccaccg acg 33
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 131
LENGTH: 32
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 131
cgctgggcag agctacttga cggtgacggt gg 32
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 132
LENGTH: 36
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 132
ggcgccggca agcttgccat gacagagcag cagtgg 36
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 133
LENGTH: 26
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 133
cgaactcgcc ggatcccgtg tttcgc 26
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 134
LENGTH: 32
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 134
ggcaaccgcg agatctttct cccggccggg gc 32
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 135
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 135
ggcaagcttg ccggcgccta acgaact 27
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 136
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 136

ggacccagat ctatgacaga gcagcagtgg 30
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 137
LENGTH: 47
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 137
ccggcagccc cggccgggag aaaagctttg cgaacatccc agtgacg 47
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 138
LENGTH: 44
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 138
gttcgcaaag cttttctccc ggccggggct gccggtcgag tacc 44
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 139
LENGTH: 20
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 139
ccttcggtgg atcccgtcag 20
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 140
LENGTH: 450
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 140
tggcgctgtc accgaggaac ctgtcaatgt cgtcgagcag tactgaaccg ttccgagaaa 60
ggccagcatg aacgtcaccg tatccattcc gaccatcctg cggccccaca ccggcggcca 120
gaagagtgtc tcggccagcg gcgatacctt gggtgccgtc atcagcgacc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 141
LENGTH: 93
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 141
Met Asn Val Thr Val Ser Ile Pro Thr Ile Leu Arg Pro His Thr Gly
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 142
LENGTH: 480
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 142
ggtgttcccg cggccggcta tgacaacagt caatgtgcat gacaagttac aggtattagg 60
tccaggttca acaaggagac aggcaacatg gcaacacgtt ttatgacgga tccgcacgcg 120
atgcgggaca tggcgggccg ttttgaggtg cacgcccaga cggtggagga. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 143
LENGTH: 98
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 143
Met Ala Thr Arg Phe Met Thr Asp Pro His Ala Met Arg Asp Met Ala
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 144
LENGTH: 940
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 144
gccccagtcc tcgatcgcct catcgccttc accggccgcc agccgaccgc aggccacgtg 60
tccgccacct aacgaaagga tgatcatgcc caagagaagc gaatacaggc aaggcacgcc 120
gaactgggtc gaccttcaga ccaccgatca gtccgccgcc aaaaagttct. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 145
LENGTH: 261

TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 145
Met Pro Lys Arg Ser Glu Tyr Arg Gln Gly Thr Pro Asn Trp Val Asp
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 146
LENGTH: 280
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 146
ccgaaaggcg gtgcaccgca cccagaagaa aaggaaagat cgagaaatgc cacagggaac 60
tgtgaagtgg ttcaacgcgg agaaggggtt cggctttatc gcccccgaag acggttccgc 120
ggatgtattt gtccactaca cggagatcca gggaacgggc ttccgcaccc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 147
LENGTH: 67
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 147
Met Pro Gln Gly Thr Val Lys Trp Phe Asn Ala Glu Lys Gly Phe Gly
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 148
LENGTH: 540
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 148
atcgtgtcgt atcgagaacc ccggccggta tcagaacgcg ccagagcgca aacctttata 60
acttcgtgtc ccaaatgtga cgaccatgga ccaaggttcc tgagatgaac ctacggcgcc 120
atcagaccct gacgctgcga ctgctggcgg catccgcggg cattctcagc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 149
LENGTH: 129
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 149
Met Asn Leu Arg Arg His Gln Thr Leu Thr Leu Arg Leu Leu Ala Ala
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 150
LENGTH: 400
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 150
atagtttggg gaaggtgtcc ataaatgagg ctgtcgttga ccgcattgag cgccggtgta 60
ggcgccgtgg caatgtcgtt gaccgtcggg gccggggtcg cctccgcaga tcccgtggac 120
gcggtcatta acaccacctg caattacggg caggtagtag ctgcgctcaa. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 151
LENGTH: 110
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 151
Met Arg Leu Ser Leu Thr Ala Leu Ser Ala Gly Val Gly Ala Val Ala
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 152
LENGTH: 990
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 152
aatagtaata tcgctgtgcg gttgcaaaac gtgtgaccga ggttccgcag tcgagcgctg 60
cgggccgcct tcgaggagga cgaaccacag tcatgacgaa catcgtggtc ctgatcaagc 120
aggtcccaga tacctggtcg gagcgcaagc tgaccgacgg cgatttcacg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 153
LENGTH: 266

TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 153
Met Thr Asn Ile Val Val Leu Ile Lys Gln Val Pro Asp Thr Trp Ser
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 154
LENGTH: 25
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 154
ctgagatcta tgaacctacg gcgcc 25
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 155
LENGTH: 35
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 155
ctcccatggt accctaggac ccgggcagcc ccggc 35
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 156
LENGTH: 29
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 156
ctgagatcta tgaggctgtc gttgaccgc 29
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 157
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 157
ctccccgggc ttaatagttg ttgcaggagc 30
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 158
LENGTH: 33
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 158
gcttagatct atgattttct gggcaaccag gta 33
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 159
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 159
gcttccatgg gcgaggcaca ggcgtgggaa 30
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 160
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 160
ctgagatcta gaatgccaca gggaactgtg 30
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 161
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 161
tctcccgggg gtaactcaga gcgagcggac 30
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 162
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 162
ctgagatcta tgaacgtcac cgtatcc 27

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 163
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 163
tctcccgggg ctcacccacc ggccacg 27
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 164
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 164
ctgagatcta tggcaacacg ttttatgacg 30
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 165
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 165
ctccccgggt tagctgctga ggatctgcth 30
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 166
LENGTH: 31
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 166
ctgaagatct atgcccaaga gaagcgaata c 31
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 167
LENGTH: 31
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 167
cggcagctgc tagcattctc cgaatctgcc g 31
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 168
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 168
Pro Gln Gly Thr Val Lys Trp Phe Asn Ala Glu Lys Gly Phe Gly
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 169
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: UNSURE
LOCATION: (15)
OTHER INFORMATION: Xaa is unknown
SEQUENCE: 169
Asn Val Thr Val Ser Ile Pro Thr Ile Leu Arg Pro Xaa. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 170
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: VARIANT
LOCATION: (1)
OTHER INFORMATION: Thr could also be Ala
SEQUENCE: 170
Thr Arg Phe Met Thr Asp Pro His Ala Met Arg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 171
LENGTH: 15

TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 171
Pro Lys Arg Ser Glu Tyr Arg Gln Gly Thr Pro Asn Trp Val Asp
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 172
LENGTH: 404
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 172
Met Ala Thr Val Asn Arg Ser Arg His His His His His His His His
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 173
LENGTH: 403
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 173
Met Ala Thr Val Asn Arg Ser Arg His His His His His His His His
1 5. . .
CLM What is claimed is:
. . . in a) with respect to the ability of evoking a protective immune response against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex, or c) comprises an amino acid sequence having a sequence identity with the polypeptide defined in a) or the. . . in a) with respect to the ability of evoking a protective immune response against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex, with the proviso that i) the polypeptide fragment is in essentially pure form when consisting of the amino acid. . .

. . . weeks of primary infection or within 4 days after the mouse has been rechallenge infected with mycobacteria belonging to the **tuberculosis** complex, the induction performed by the addition of the polypeptide to a suspension comprising about 200.000 spleen cells per ml,. . . suspension; and/or 3) induces an IFN-γ release from bovine PBMC derived from animals previously sensitized with mycobacteria belonging to the **tuberculosis** complex, said release being at least two times the release observed from bovine PBMC derived from animals not previously sensitized with mycobacteria belonging to the **tuberculosis** complex.

. . . fragment as defined in any of claims 1-8, and an other polypeptide fragment derived from a bacterium belonging to the **tuberculosis** complex, such as ESAT-6 or at least one T-cell epitope thereof, MPB64 or at least one T-cell epitope thereof, MPT64. . .

. . . first amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. **tuberculosis** protein ESAT-6, and a second amino acid sequence including at least one T-cell epitope derived from a M. **tuberculosis** protein different from ESAT-6 and/or including a stretch of amino acids which protects the first amino acid sequence from in. . . first amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. **tuberculosis** protein MPT59, and a second amino acid sequence including at least one T-cell epitope derived from a M. **tuberculosis** protein different from MPT59 and/or including a stretch of amino acids which protects the first amino acid sequence from in. . .

. . . 11-13, wherein the at least one T-cell epitope included in the second amino acid sequence is derived from a M. **tuberculosis** polypeptide selected from the group consisting of a polypeptide fragment

according to any of claims 1-55, DnaK, GroEL, urease, glutamine. . .
. . . sequence of ESAT-6 or of MPT59 and/or the second amino acid sequence is the amino acid sequence of a M. **tuberculosis** polypeptide selected from the group consisting of a polypeptide fragment according to any of claims 1-8, DnaK, GroEL, urease, glutamine. . .
. . . according to any of claims 1-20 in the preparation of a pharmaceutical composition for the diagnosis of or vaccination against **tuberculosis** caused by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis.

. . . been administered, the amount of expressed antigen being effective to confer substantially increased resistance to infections with mycobacteria of the **tuberculosis** complex in an animal, including a human being.

. . . according to claim 23 or 24 in the preparation of a pharmaceutical composition for the diagnosis of or vaccination against **tuberculosis** caused by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis.

35. A vaccine for immunizing an animal, including a human being, against **tuberculosis** caused by mycobacteria belonging to the **tuberculosis** complex, comprising as the effective component a non-pathogenic microorganism, wherein at least one copy of a DNA fragment comprising a. . .
44. A transformed cell according to claim 43, which is a bacterium belonging to the **tuberculosis** complex, such as a M. **tuberculosis** bovis BCG cell.

. . . polypeptide from a short-term culture filtrate as defined in claim 1; or isolating the polypeptide from whole mycobacteria of the **tuberculosis** complex or from lysates or fractions thereof, e.g. cell wall containing fractions; or synthesizing the polypeptide by solid or liquid. . .
. . . of claims 1-20, and solubilizing or dispersing the polypeptide in a medium for a vaccine, and optionally adding other M. **tuberculosis** antigens and/or a carrier, vehicle and/or adjuvant substance, or cultivating a cell according to any of claims 37-45, and transferring. . .
48. A method of diagnosing **tuberculosis** caused by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis in an animal, including a human being, comprising intradermally injecting, in the animal, a polypeptide. . . composition according to claim 34, a positive skin response at the location of injection being indicative of the animal having **tuberculosis**, and a negative skin response at the location of injection being indicative of the animal not having **tuberculosis**
.

49. A method for immunising an animal, including a human being, against **tuberculosis** caused by mycobacteria belonging to the **tuberculosis** complex, comprising administering to the animal the polypeptide according to any of claims 1-20, the immunologic composition according to claim. . .
. . . A method for diagnosing ongoing or previous sensitization in an animal or a human being with bacteria belonging to the **tuberculosis** complex, the method comprising providing a blood sample from the animal or human being, and contacting the sample from the. . .
52. A composition for diagnosing **tuberculosis** in an animal, including a human being, comprising a polypeptide according to any of claims 1-20, or a nucleic acid. . .

```
=>      e skjot rikke/au
E1            2     SKJOT R L/AU
E2            9     SKJOT R L V/AU
E3            1 --> SKJOT RIKKE/AU
```

```
E4            2     SKJOT RIKKE L V/AU
E5           17     SKJOT RIKKE LOUISE VINTHER/AU
E6            1     SKJOT V/AU
E7           11     SKJOTH C A/AU
E8            5     SKJOTH C AMBELAS/AU
E9            4     SKJOTH CARSTEN AMBELAS/AU
E10          22     SKJOTH F/AU
E11           4     SKJOTH FLEMMING/AU
E12           4     SKJOTH L/AU

=> s e1-e5 and tuberculosis
L4           31 ("SKJOT R L"/AU OR "SKJOT R L V"/AU OR "SKJOT RIKKE"/AU OR "SKJO
                T RIKKE L V"/AU OR "SKJOT RIKKE LOUISE VINTHER"/AU) AND TUBERCUL
                OSIS

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5           11 DUP REM L4 (20 DUPLICATES REMOVED)

=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 11 ANSWERS - CONTINUE? Y/(N):y


L5   ANSWER 1 OF 11  CAPLUS  COPYRIGHT 2005 ACS on STN DUPLICATE 1
AN   2004:59568  CAPLUS
DN   140:127185
TI   Antigens from Mycobacterium as vaccine and uses in tuberculosis
     diagnosis and treatment
IN   Andersen, Peter; Skjot, Rikke Louise Vinther; Okkels, Li Mei
     Meng; Brock, Inger; Oettinger, Thomas
PA   Den.
SO   U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 804,980.
     CODEN: USXXCO
DT   Patent
LA   English
FAN.CNT 10
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     --------------      ----   --------    --------------------   --------
PI   US 2004013685        A1    20040122    US 2001-872505         20010601
     EP 1449922           A2    20040825    EP 2004-76605          19980401
     EP 1449922           A3    20041117
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI, CY
     WO 2001004151        A2    20010118    WO 2000-DK398          20000713
     WO 2001004151        A3    20010712
         W:  AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
             CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI,
             GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
             KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX,
             MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM,
             TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,
             MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     US 2003147897        A1    20030807    US 2001-804980         20010313
PRAI DK 1997-1277         A     19971110
     US 1998-70488P       P     19980105
     US 1998-246191       B2    19981230
     DK 1999-1020         A     19990713
     US 1999-144011P      P     19990715
     US 2000-615947       A2    20000713
     WO 2000-DK398        A2    20000713
     US 2001-804980       A2    20010313
     DK 1993-798          A     19930702
     US 1993-123182       B2    19930920
     WO 1994-DK273        A2    19940701
     US 1995-465640       A1    19950605
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	DK 1997-376	A	19970402
	US 1997-44624P	P	19970418
	EP 1998-913536	A3	19980401
	US 1999-289388	B2	19990412

AB The present invention is based on the identification and characterization of 3 antigens, including Rv2653c, Rv2654c and RD1-ORF5, from Mycobacterium **tuberculosis**. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing **tuberculosis** caused by virulent mycobacteria in an animal, including a human being. The invention related to treating **tuberculosis** using antigens isolated from Mycobacterium **tuberculosis**.

L5 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2
AN 2003:696302 CAPLUS
DN 139:229237
TI Protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment
IN Andersen, Peter; Weldingh, Karin; Hansen, Christina Veggerby; Florio, Walter; Okkels, Li Mei Meng; **Skjot, Rikke Louise Vinther**; Rasmussen, Peter Birk
PA Den.
SO U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Ser. No. 60,428. CODEN: USXXCO
DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003165525	A1	20030904	US 2002-138473	20020502
	US 6641814	B1	20031104	US 1998-50739	19980330
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	US 2002094336	A1	20020718	US 2001-791171	20010220
PRAI	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-50739	A2	19980330		
	DK 1998-1281	A	19981008		
	US 2001-791171	B2	20010220		
	US 2002-60428	A2	20020129		
	EP 1998-913536	A3	19980401		

AB The present invention is based on the identification and characterization of 9 antigens, including Rv0652/CFP16, Rv2462c/TB51, Rv1984c/CFP21, Rv2185c/TB16, Rv1636/TB15A, Rv3451/CFP23, Rv3872/RD1-ORF3, Rv3354/CFP8A and Rv2623/TB32, from Mycobacterium **tuberculosis**. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, in an animal, including a human being. The invention related to treating **tuberculosis** using antigens isolated from Mycobacterium **tuberculosis**.

L5 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3
AN 2003:609858 CAPLUS
DN 139:163576
TI Mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of the **tuberculosis** complex
IN Andersen, Peter; **Skjot, Rikke Louise Vinther**
PA Den.
SO U.S. Pat. Appl. Publ., 135 pp., Cont.-in-part of U.S. Ser. No. 289,388,

abandoned.
CODEN: USXXCO

DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003147897	A1	20030807	US 2001-804980	20010313
	WO 9501441	A1	19950112	WO 1994-DK273	19940701
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, CZ, DE, DE, DK, DK, ES, FI, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, SK, TJ, TT, UA				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	EP 1508339	A1	20050223	EP 2004-77505	19940701
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI				
	US 5955077	A	19990921	US 1995-465640	19950605
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	US 2004013685	A1	20040122	US 2001-872505	20010601
PRAI	DK 1993-798	A	19930702		
	US 1993-123182	B2	19930920		
	WO 1994-DK273	A2	19940701		
	US 1995-465640	A1	19950605		
	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1999-289388	B2	19990412		
	EP 1994-919574	A3	19940701		
	EP 1998-913536	A3	19980401		
	US 1998-246191	B2	19981230		
	DK 1999-1020	A	19990713		
	US 1999-144011P	P	19990715		
	US 2000-615947	A2	20000713		
	WO 2000-DK398	A2	20000713		
	US 2001-804980	A2	20010313		

AB The present invention is based on the identification and characterization of a number of novel M. **tuberculosis** derived proteins and protein fragments, e.g. TB10.3 (ORF7-1 or Rv3019c), TB10.4 (CFP7 or Rv0288) and TB12.9 (ORF7-2 or Rv3017c), ESAT-6, MPT64, CFP10, RD1-ORF5, RD1-ORF2, Rv1036, Ag85A, Ag85B, Ag85C, 19 kDa lipoprotein, MPT32, MPB59 and α-crystallin. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides.

L5 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4
AN 2002:906996 CAPLUS
DN 138:13499
TI Hybrids of M. **tuberculosis** antigens used as vaccines
IN Andersen, Peter; Olsen, Anja Weinreich; **Skjot, Rikke Louise Vinther**; Rasmussen, Peter Birk
PA Den.
SO U.S. Pat. Appl. Publ., 36 pp., Cont.-in-part of U.S. Ser. No. 246,191, abandoned.
CODEN: USXXCO

DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002176867	A1	20021128	US 2001-805427	20010313
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY

PRAI US 1997-44624P P 19970418
DK 1997-1277 A 19971110
US 1998-70488P P 19980105
US 1998-246191 B2 19981230
DK 1997-376 A 19970402
EP 1998-913536 A3 19980401

AB The invention discloses fusion proteins consisting of T cell epitopes derived from the immunodominant antigens ESAT-6 and Ag85B from Mycobacterium **tuberculosis** or homologs thereof, and a **tuberculosis** vaccine based on the fusion proteins, which induces efficient immunol. memory. It is preferred that the sequences of the first and second T cell epitopes each have a sequence identity of at least 70% with the natively occurring sequence in the proteins from which they are derived. In the most preferred embodiment, the fusion polypeptide comprises ESAT-6 fused to Ag85B wherein ESAT-6 is fused to the C terminus of Ag85B. In one embodiment, there are nitric oxide linkers introduced between the 2 amino acid sequences constituting the parent polypeptide fragments.

L5 ANSWER 5 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 5
AN 2002:559608 BIOSIS
DN PREV200200559608
TI Epitope mapping of the immunodominant antigen TB10.4 and the two homologous proteins TB10.3 and TB12.9, which constitute a subfamily of the esat-6 gene family.
AU **Skjot, Rikke Louise Vinther**; Brock, Inger; Arend, Sandra M.; Munk, Martin E.; Theisen, Michael; Ottenhoff, Tom H. M.; Andersen, Peter [Reprint author]
CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen S, Denmark
pa@ssi.dk
SO Infection and Immunity, (October, 2002) Vol. 70, No. 10, pp. 5446-5453. print.
CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 30 Oct 2002
Last Updated on STN: 30 Oct 2002
AB The human T-cell recognition of the low-molecular-mass culture filtrate antigen TB10.4 was evaluated in detail. The molecule was strongly recognized by T cells isolated from **tuberculosis** (TB) patients and from BCG-vaccinated donors. The epitopes on TB10.4 were mapped with overlapping peptides and found to be distributed throughout the molecule. The broadest response was found in TB patients, whereas the response in BCG-vaccinated donors was focused mainly toward a dominant epitope located in the N terminus (amino acids 1 to 18). The gene encoding TB10.4 was found to belong to a subfamily within the esat-6 family that consists of the three highly homologous proteins TB10.4, TB10.3, and TB12.9 (Rv0288, Rv3019c, and Rv3017c, respectively). Southern blot analysis combined with database searches revealed that the three members of the TB10.4 family were present only in strains of the Mycobacterium **tuberculosis** complex, including BCG, and M. kansasii, whereas other atypical mycobacteria had either one (M. avium, M. intracellulare, and M. marinum) or none (M. scrofulaceum, M. fortuitum, and M. szulgai) of the genes. The fine specificity of the T-cell response to the three closely related esat-6 family members was markedly different, with only a few epitopes shared between the molecules. Minimal differences in the amino acid sequence translated into large differences in recognition by T cells and secretion of gamma interferon. In general, the peptides from TB10.4 stimulated the largest responses, but epitopes unique to both TB10.3 and TB12.9 were found. The relevance of the findings for TB vaccine development and as a potential mechanism for immune evasion is discussed.

L5 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:50676 CAPLUS

DN 134:114829.
TI **Tuberculosis** vaccine and diagnostics based on the Mycobacterium **tuberculosis** esat-6 gene family
IN Andersen, Peter; **Skjot, Rikke**
PA Statens Serum Institut, Den.
SO PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001004151	A2	20010118	WO 2000-DK398	20000713
	WO 2001004151	A3	20010712		
	W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2378763	AA	20010118	CA 2000-2378763	20000713
	EP 1200466	A2	20020502	EP 2000-945660	20000713
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003510018	T2	20030318	JP 2001-509760	20000713
	AU 779495	B2	20050127	AU 2000-59664	20000713
	US 2004013685	A1	20040122	US 2001-872505	20010601
PRAI	DK 1999-1020	A	19990713		
	US 1999-144011P	P	19990715		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-246191	B2	19981230		
	US 2000-615947	A2	20000713		
	WO 2000-DK398	W	20000713		
	US 2001-804980	A2	20010313		

AB The authors report the cloning and T-cell-stimulatory activity of members of the esat-6 gene family of Mycobacterium **tuberculosis**.

L5 ANSWER 7 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 6
AN 2001:534626 BIOSIS
DN PREV200100534626
TI Antigen discovery and **tuberculosis** vaccine development in the post-genomic era.
AU **Skjot, Rikke Louise Vinther**; Agger, Else Marie; Andersen, Peter [Reprint author]
CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen, Denmark
SO Scandinavian Journal of Infectious Diseases, (2001) Vol. 33, No. 9, pp. 643-647. print.
CODEN: SJIDB7. ISSN: 0036-5548.
DT Article
LA English
ED Entered STN: 14 Nov 2001
Last Updated on STN: 23 Feb 2002
AB For a number of years, a major effort has been put into the identification of candidate molecules for inclusion in a novel vaccine against **tuberculosis**. Various techniques have been exploited and have resulted in the identification of immunologically important antigens such as the immunodominant antigens ESAT-6 and antigen 85A/B. Today, the availability of the total nucleotide sequence of the Mycobacterium **tuberculosis** genome enables a post-genomic antigen discovery approach based on denotation and screening of complete protein families containing immunodominant molecules. One group of genes sharing

properties with ESAT-6 constitute what has been called the esat-6 gene family. The genes have 10-35% homology to esat-6, are approximately the same size and share genomic organization. The data accumulated so far demonstrate that these molecules are immunodominant antigens strongly recognized in human TB patients and with the potential for a novel TB vaccine.

L5 ANSWER 8 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2003:208455 BIOSIS
DN PREV200300208455
TI Antigen discovery and **tuberculosis** vaccine development in the post-genomic era.
AU **Skjot, Rikke Louise Vinther**; Agger, Else Marie; Andersen, Peter [Reprint Author]
CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen, Denmark
SO Scandinavian Journal of Infectious Diseases, (2001) No. Special Issue, pp. 79-83. print.
CODEN: SJIDB7. ISSN: 0036-5548.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 30 Apr 2003
Last Updated on STN: 30 Apr 2003
AB For a number of years, a major effort has been put into the identification of candidate molecules for inclusion in a novel vaccine against **tuberculosis**. Various techniques have been exploited and have resulted in the identification of immunologically important antigens such as the immunodominant antigens ESAT-6 and antigen 85A/B. Today, the availability of the total nucleotide sequence of the Mycobacterium **tuberculosis** genome enables a post-genomic antigen discovery approach based on denotation and screening of complete protein families containing immunodominant molecules. One group of genes sharing properties with ESAT-6 constitute what has been called the esat-6 gene family. The genes have 10-35% homology to esat-6, are approximately the same size and share genomic organization. The data accumulated so far demonstrate that these molecules are immunodominant antigens strongly recognized in human TB patients and with the potential for a novel TB vaccine.

L5 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:260319 CAPLUS
DN 132:292711
TI Tb vaccine and diagnostic based on antigens from the Mycobacterium **tuberculosis** cell
IN Andersen, Peter; Weldingh, Karin; Hansen, Christina Veggerby; Florio, Walter; Okkels, Li Mei Meng; **Skjot, Rikke Louise Vinther**; Rosenkrands, Ida
PA Statens Serum Institut, Den.
SO PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 10

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000021983	A2	20000420	WO 1999-DK538	19991008
WO 2000021983	A3	20001123		
W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2346218	AA	20000420	CA 1999-2346218	19991008

AU 9960784 A1 20000501 AU 1999-60784 19991008
AU 766093 B2 20031009
EP 1117683 A2 20010725 EP 1999-947257 19991008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, IE, SI, LT, LV, FI, RO
PRAI DK 1998-1281 A 19981008
US 1999-116673P P 19990121
WO 1999-DK538 W 19991008
AB The present invention relates to substantially pure polypeptides, which has a sequence identity of at least 80 % to an amino acid sequence disclosed, or which is a subsequence of at least 6 amino acids thereof, preferably a B- or T-cell epitope of the polypeptides disclosed. The polypeptide or the subsequence thereof has at least one of nine properties. The use of the disclosed polypeptides in medicine is disclosed, preferably as vaccine or diagnostic agents relating to virulent Mycobacterium. The invention further relates to the nucleotide sequences disclosed and the nucleotide sequences encoding the disclosed polypeptides. Medical and non-medical use of the nucleotide sequences is disclosed.

L5 ANSWER 10 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 7
AN 2000:349404 BIOSIS
DN PREV200000349404
TI Detection of active **tuberculosis** infection by T cell responses to early-secreted antigenic target 6-kDa protein and culture filtrate protein 10.
AU Arend, Sandra M. [Reprint author]; Andersen, Peter; van Meijgaarden, Krista E.; **Skjot, Rikke L. V.**; Subronto, Yanri W.; van Dissel, Jaap T.; Ottenhoff, Tom H. M.
CS Dept. of Infectious Diseases, C5P, Leiden University Medical Center, 2300 RC, Leiden, Netherlands
SO Journal of Infectious Diseases, (May, 2000) Vol. 181, No. 5, pp. 1850-1854. print.
CODEN: JIDIAQ. ISSN: 0022-1899.
DT Article
LA English
ED Entered STN: 16 Aug 2000
Last Updated on STN: 7 Jan 2002
AB The purified protein derivative (PPD) skin test has no predictive value for **tuberculosis** (TB) in Mycobacterium bovis bacillus Calmette-Guerin (BCG)-vaccinated individuals because of cross-reactive responses to nonspecific constituents of PPD. T cell responses to early-secreted antigenic target 6-kDa protein (ESAT-6) and the newly identified culture filtrate protein 10 (CFP-10), 2 proteins specifically expressed by M. **tuberculosis** (MTB) but not by BCG strains, were evaluated. Most TB patients responded to ESAT-6 (92%) or CFP-10 (89%). A minority of BCG-vaccinated individuals responded to both ESAT-6 and CFP-10, their history being consistent with latent infection with MTB in the presence of protective immunity. No responses were found in PPD-negative controls. The sensitivity and specificity of the assay were 84% and 100%, respectively, at a cutoff of 300 pg of interferon-gamma/mL. These data indicate that ESAT-6 and CFP-10 are promising antigens for highly specific immunodiagnosis of TB, even in BCG-vaccinated individuals.

L5 ANSWER 11 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 8
AN 2000:104643 BIOSIS
DN PREV200000104643
TI Comparative evaluation of low-molecular-mass proteins from Mycobacterium **tuberculosis** identifies members of the ESAT-6 family as immunodominant T-cell antigens.
AU **Skjot, Rikke Louise Vinther**; Oettinger, Thomas; Rosenkrands, Ida; Ravn, Pernille; Brock, Inger; Jacobsen, Susanne; Andersen, Peter [Reprint author]
CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen S, Denmark
SO Infection and Immunity, (Jan., 2000) Vol. 68, No. 1, pp. 214-220. print.

CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 22 Mar 2000
Last Updated on STN: 3 Jan 2002
AB Culture filtrate from Mycobacterium **tuberculosis** contains protective antigens of relevance for the generation of a new antituberculosis vaccine. We have identified two previously uncharacterized M. **tuberculosis** proteins (TB7.3 and TB10.4) from the highly active low-mass fraction of culture filtrate. The molecules were characterized, mapped in a two-dimensional electrophoresis reference map of short-term culture filtrate, and compared with another recently identified low-mass protein, CFP10 (F. X. Berthet, P. B. Rasmussen, I. Rosenkrands, P. Andersen, and B. Gicquel. Microbiology 144:3195-3203, 1998), and the well-described ESAT-6 antigen. Genetic analyses demonstrated that TB10.4 as well as CFP10 belongs to the ESAT-6 family of low-mass proteins, whereas TB7.3 is a low-molecular-mass protein outside this family. The proteins were expressed in Escherichia coli, and their immunogenicity was tested in cultures of peripheral blood mononuclear cells from human **tuberculosis** (TB) patients, Mycobacterium bovis BCG-vaccinated donors, and nonvaccinated donors. The two ESAT-6 family members, TB10.4 and CFP10, were very strongly recognized and induced gamma interferon release at the same level (CFP10) as or at an even higher level (TB10.4) than ESAT-6. The non-ESAT-6 family member, TB7.3, for comparison, was recognized at a much lower level. CFP10 was found to distinguish TB patients from BCG-vaccinated donors and is, together with ESAT-6, an interesting candidate for the diagnosis of TB. The striking immunodominance of antigens within the ESAT-6 family is discussed, and hypotheses are presented to explain this targeting of the immune response during TB infection.

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=> e okkels li mei/au
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E3            0 --> OKKELS LI MEI/AU
E4            6     OKKELS LI MEI MENG/AU
E5            4     OKKELS LIMEI M/AU
E6           22     OKKELS LIMEI MENG/AU
E7            2     OKKELS S/AU
E8            4     OKKELS SIGURD/AU
E9            1     OKKELS THYGE FINN/AU
E10           1     OKKEMA A/AU
E11           4     OKKEMA A T/AU
E12          40     OKKEMA A Z/AU

=> s e2-e6 and tuberculosis
L6           55 ("OKKELS L M"/AU OR "OKKELS LI MEI"/AU OR "OKKELS LI MEI MENG"/A
                U OR "OKKELS LIMEI M"/AU OR "OKKELS LIMEI MENG"/AU) AND TUBERCUL
                OSIS

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7            13 DUP REM L6 (42 DUPLICATES REMOVED)

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YOU HAVE REQUESTED DATA FROM 13 ANSWERS - CONTINUE? Y/(N):y

L7   ANSWER 1 OF 13  CAPLUS  COPYRIGHT 2005 ACS on STN DUPLICATE 1
AN   2005:119461  CAPLUS
DN   142:334537
TI   Assessing the serodiagnostic potential of 35 Mycobacterium
     tuberculosis proteins and identification of four novel serological
     antigens
AU   Weldingh, Karin; Rosenkrands, Ida; Okkels, Limei Meng; Doherty,
     T. Mark; Andersen, Peter
CS   Department of Infectious Disease Immunology, Statens Serum Institut,
     Copenhagen, Den.
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SO Journal of Clinical Microbiology (2005), 43(1), 57-65
CODEN: JCMIDW; ISSN: 0095-1137
PB American Society for Microbiology
DT Journal
LA English
AB Improved diagnostic reagents are needed for the detection of Mycobacterium **tuberculosis** infections, and the development of a serodiagnostic test would complement presently available diagnostic methods. The aim of the present study was to identify novel serol. targets for use for the future serodiagnosis of **tuberculosis** (TB). The authors cloned and expressed 35 M. **tuberculosis** proteins as recombinant proteins in Escherichia coli and analyzed their serodiagnostic potentials. By a two-step selection process, four superior seroantigens, TB9.7, TB15.3, TB16.3, and TB51, were identified, none of which has been described before. The four novel antigens were tested with panels of sera from smear-pos. and smear-neg. TB patients from areas both where TB is endemic and where TB is not endemic, with recognition frequencies ranging from 31 to 93% and with a specificity of at least 97%. The single most potent antigen was TB16.3, which had a sensitivity of 48 to 55% with samples from Danish resident TB patients and a sensitivity of 88 to 98% with samples from African TB patients. Importantly, the TB16.3 and the TB9.7 antigens were recognized by more than 85% of the samples from TB patients coinfected with human immunodeficiency virus, a patient group for which it is in general difficult to detect M. **tuberculosis** -specific antibodies.
RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2
AN 2004:59568 CAPLUS
DN 140:127185
TI Antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment
IN Andersen, Peter; Skjot, Rikke Louise Vinther; **Okkels, Li Mei Meng** ; Brock, Inger; Oettinger, Thomas
PA Den.
SO U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 804,980.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004013685	A1	20040122	US 2001-872505	20010601
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	WO 2001004151	A2	20010118	WO 2000-DK398	20000713
	WO 2001004151	A3	20010712		
	W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2003147897	A1	20030807	US 2001-804980	20010313
PRAI	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-246191	B2	19981230		
	DK 1999-1020	A	19990713		
	US 1999-144011P	P	19990715		
	US 2000-615947	A2	20000713		
	WO 2000-DK398	A2	20000713		

	US 2001-804980	A2	20010313
	DK 1993-798	A	19930702
	US 1993-123182	B2	19930920
	WO 1994-DK273	A2	19940701
	US 1995-465640	A1	19950605
	DK 1997-376	A	19970402
	US 1997-44624P	P	19970418
	EP 1998-913536	A3	19980401
	US 1999-289388	B2	19990412

AB The present invention is based on the identification and characterization of 3 antigens, including Rv2653c, Rv2654c and RD1-ORF5, from Mycobacterium **tuberculosis**. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing **tuberculosis** caused by virulent mycobacteria in an animal, including a human being. The invention related to treating **tuberculosis** using antigens isolated from Mycobacterium **tuberculosis**.

L7 ANSWER 3 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 3
AN 2005:31533 BIOSIS
DN PREV200500031352
TI Protective effect of a **tuberculosis** subunit vaccine based on a fusion of antigen 85B and ESAT-6 in the aerosol guinea pig model.
AU Olsen, Anja W.; Williams, Ann; **Okkels, Limei M.**; Hatch, Graham; Andersen, Peter [Reprint Author]
CS Dept Infect Dis Immunol, Statens Serum Inst, Artillerivej 5, DK-2300, Copenhagen, S, Denmark
pa@ssi.dk
SO Infection and Immunity, (October 2004) Vol. 72, No. 10, pp. 6148-6150. print.
ISSN: 0019-9567 (ISSN print).
DT Article
LA English
ED Entered STN: 12 Jan 2005
Last Updated on STN: 12 Jan 2005
AB A fusion protein of antigen 85B (Ag85B) and ESAT-6 administered in cationic lipid vesicles conferred a highly significant level of protection against Mycobacterium **tuberculosis** in the guinea pig aerosol model of infection. The protection was manifested as delayed clinical illness and prolonged survival. Neither Ag85B nor ESAT-6 (independently or as a cocktail) induced significant protection in this model.

L7 ANSWER 4 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 4
AN 2005:26452 BIOSIS
DN PREV200500027841
TI CFP10 discriminates between nonacetylated and acetylated ESAT-6 of Mycobacterium **tuberculosis** by differential interaction.
AU **Okkels, Limei Meng**; Mueller, Eva-Christina; Schmid, Monika; Rosenkrands, Ida; Kaufmann, Stefan H. E.; Andersen, Peter; Jungblut, Peter R. [Reprint Author]
CS Core Facil Prot Anal, Max Planck Inst Infect Biol, Schumannstr 21-22, D-10117, Berlin, Germany
jungblut@mpiib-berlin.mpg.de
SO Proteomics, (October 2004) Vol. 4, No. 10, pp. 2954-2960. print.
ISSN: 1615-9853 (ISSN print).
DT Article
LA English
ED Entered STN: 5 Jan 2005
Last Updated on STN: 5 Jan 2005
AB ESAT-6 (the 6 kDa early secreted antigenic target) protein species in short-term culture filtrate of Mycobacterium **tuberculosis** were separated in a 4-5 narrow range p/ gradient two-dimensional gel electrophoresis (2-DE). Eight ESAT-6 protein species were analyzed in detail by peptide mass fingerprinting matrix-assisted laser desorption/ionization-mass spectrometry as well as by electrospray

ionization-tandem mass spectrometry. An N-terminal Thr acetylation was identified in four species and a C-terminal truncation was identified in two species. In 2-DE blot overlay assays, the recombinant 10 kDa culture filtrate protein (CFP10) discriminated N-terminal acetylated and nonacetylated ESAT-6 by differential interaction, whereas removal of the C-terminal 11 residues of ESAT-6 had no effects thereon. This example shows that the access to the protein species level can be a prerequisite to understand regulation of protein-protein interaction.

L7 ANSWER 5 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 5
AN 2004:307035 BIOSIS
DN PREV200400304119
TI Protein-protein interactions of proteins from the ESAT-6 family of Mycobacterium **tuberculosis**.
AU **Okkels, Limei Meng** [Reprint Author]; Andersen, Peter
CS Max Planck Inst Infect Biol, Schumannstr 21-22, D-10117, Berlin, Germany
okkels@mpiib-berlin.mpg.de
SO Journal of Bacteriology, (April 2004) Vol. 186, No. 8, pp. 2487-2491.
print.
CODEN: JOBAAY. ISSN: 0021-9193.
DT Article
LA English
ED Entered STN: 7 Jul 2004
Last Updated on STN: 7 Jul 2004
AB In the present study, we demonstrate that, in analogy with the genes encoding ESAT-6 and CFP-10, the genes rv0287 and rv0288 from the ESAT-6 gene family are cotranscribed. Using Western-Western blotting and protein-print overlay methodologies, we demonstrate that ESAT-6 and CFP-10, as well as the protein pair Rv0288/Rv0287, interact pairwise in a highly specific way. Most notably, the ESAT-6 proteins interact directly with Rv3873, a possible cell envelope component of the ESAT-6 secretion pathway.

L7 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 6
AN 2003:696302 CAPLUS
DN 139:229237
TI Protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment
IN Andersen, Peter; Weldingh, Karin; Hansen, Christina Veggerby; Florio, Walter; **Okkels, Li Mei Meng**; Skjot, Rikke Louise Vinther; Rasmussen, Peter Birk
PA Den.
SO U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Ser. No. 60,428.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003165525	A1	20030904	US 2002-138473	20020502
	US 6641814	B1	20031104	US 1998-50739	19980330
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	US 2002094336	A1	20020718	US 2001-791171	20010220
PRAI	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-50739	A2	19980330		
	DK 1998-1281	A	19981008		
	US 2001-791171	B2	20010220		
	US 2002-60428	A2	20020129		
	EP 1998-913536	A3	19980401		

AB The present invention is based on the identification and characterization of 9 antigens, including Rv0652/CFP16, Rv2462c/TB51, Rv1984c/CFP21,

Rv2185c/TB16, Rv1636/TB15A, Rv3451/CFP23, Rv3872/RD1-ORF3, Rv3354/CFP8A and Rv2623/TB32, from Mycobacterium **tuberculosis**. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, in an animal, including a human being. The invention related to treating **tuberculosis** using antigens isolated from Mycobacterium **tuberculosis**.

L7 ANSWER 7 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 7
AN 2004:33002 BIOSIS
DN PREV200400035432
TI PPE protein (Rv3873) from DNA segment RD1 of Mycobacterium **tuberculosis**: Strong recognition of both specific T-cell epitopes and epitopes conserved within the PPE family.
AU **Okkels, Limei Meng** [Reprint Author]; Brock, Inger; Follmann, Frank; Agger, Else Marie; Arend, Sandra M.; Ottenhoff, Tom H. M.; Oftung, Fredrik; Rosenkrands, Ida; Andersen, Peter
CS Department of Infectious Disease Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen, Denmark
lmo@ssi.dk
SO Infection and Immunity, (November 2003) Vol. 71, No. 11, pp. 6116-6123. print.
ISSN: 0019-9567 (ISSN print).
DT Article
LA English
ED Entered STN: 7 Jan 2004
Last Updated on STN: 7 Jan 2004
AB Proteins encoded by DNA segment RD1 of Mycobacterium **tuberculosis** have recently been demonstrated to play important roles in bacterial virulence, vaccine development, and diagnostic reagent design. Previously, we characterized two immunodominant T-cell antigens, the early secreted antigen target (ESAT-6),and the 10-kDa culture filtrate protein (CFP10), which are encoded by the esx-1hp operon in this region. In the present study we characterized a third putative open reading frame in this region, rv3873, which encodes a PPE protein. We found that the rv3873 gene is expressed in M. **tuberculosis** H37Rv and that the native protein, Rv3873, is predominantly associated with the mycobacterial cell or wall. When tested as a His-tagged recombinant protein, Rv3873 stimulated high levels of gamma interferon secretion in peripheral blood mononuclear cells isolated from **tuberculosis** (TB) patients, as well as from healthy tuberculin purified protein derivative-positive donors. In contrast to other RD1-encoded antigens, Rv3873 was also found to be recognized by a significant proportion of Mycobacterium bovis BCG-vaccinated donors. Epitope mapping performed with overlapping peptides revealed a broad pattern of T-cell recognition comprising both TB-specific epitopes and epitopes also recognized by BCG-vaccinated donors. The immunodominant epitope (residues 118 to 1.35) for both TB patients and BCG-vaccinated individuals was found to be highly conserved among a large number of PPE family members.

L7 ANSWER 8 OF 13 CABA COPYRIGHT 2005 CABI on STN DUPLICATE 8
AN 2003:177804 CABA
DN 20033152549
TI Genomic approach to identification of Mycobacterium bovis diagnostic antigens in cattle
AU Aagaard, C.; Govaerts, M.; **Okkels, L. M.**; Andersen, P.; Pollock, J. M.
CS Department of Infectious Disease Immunology, Statens Serum Institute, Artillerivej 5, DK-2300 Copenhagen, Denmark. caa@ssi.dk
SO Journal of Clinical Microbiology, (2003) Vol. 41, No. 8, pp. 3719-3728. 46 ref.
Publisher: American Society for Microbiology (ASM). Washington
ISSN: 0095-1137
DOI: 10.1128/JCM.41.8.3719-3728.2003

CY United States
DT Journal
LA English
ED Entered STN: 20031107
Last Updated on STN: 20031107
AB Differential delayed-type hypersensitivity skin testing with tuberculin purified protein derivatives from Mycobacterium bovis and M. avium is the standard for diagnosing bovine **tuberculosis**. However, improved tests based on defined, specific antigens are urgently needed. In the present study, a combination of bioinformatics, molecular biology, and bovine models of infection were used to screen mycobacterial proteins for their potential as diagnostic reagents which could be used in a whole-blood assay for diagnosis of **tuberculosis**. Initial screening of 28 proteins selected in silico and expressed as recombinants in Escherichia coli indicated that CFP-10, ESAT-6, TB27.4, TB16.2, TB15.8, and TB10.4 induced strong gamma interferon responses in experimentally infected cattle. A more thorough investigation over time in two groups of animals infected with a high (106 CFU) and a low (104 CFU) dose of M. bovis revealed that, for both groups, the strength of the in vitro response to individual antigens varied greatly over time. However, combining the results for ESAT-6, CFP-10, and TB27.4, possibly supplemented with TB10.4, gave sensitivities at different infection stages close to those obtained with M. bovis purified protein derivative. Importantly, while responsiveness to ESAT-6 and CFP-10 correlated strongly for individual samples, the same was not the case for ESAT-6 and TB27.4 responsiveness. The results suggest that combinations of specific antigens such as these have great potential in development of optimized diagnostic systems for bovine **tuberculosis**.

L7 ANSWER 9 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 9
AN 2004:76163 BIOSIS
DN PREV200400078267
TI Human T-cell responses to the RD1-encoded protein TB27.4 (Rv3878) from Mycobacterium **tuberculosis**.
AU Agger, Else Marie [Reprint Author]; Brock, Inger; **Okkels, Limei Meng**; Arend, Sandra M.; Aagaard, Claus S.; Weldingh, Karin N.; Andersen, Peter
CS Department of Infectious Disease Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen, S, Denmark
eag@ssi.dk
SO Immunology, (December 2003) Vol. 110, No. 4, pp. 507-512. print.
CODEN: IMMUAM. ISSN: 0019-2805.
DT Article
LA English
ED Entered STN: 4 Feb 2004
Last Updated on STN: 4 Feb 2004
AB In recent years, there has been considerable focus on the discovery and characterization of proteins derived from Mycobacterium **tuberculosis** leading to the identification of a number of candidate antigens for use in vaccine development or for diagnostic purposes. Previous experiments have demonstrated an important immunological role for proteins encoded by the RD1 region, which is absent from all strains of bacillus Calmette-Guerin (BCG) but present in the genomes of virulent M. bovis and M. **tuberculosis**. Herein, we have studied human T-cell responses to the antigen encoded by the putative open reading frame (rv3878) of the RD1 region. Immunoblot analysis revealed that rv3878 was expressed and the native protein was designated TB27.4. Immunological evaluations demonstrate that TB27.4 elicits a prominent immune response in human **tuberculosis** patients with a dominant region in the C-terminal part of the molecule. In contrast, very limited responses were seen in M. bovis BCG-vaccinated donors. This study therefore emphasizes the diagnostic potential of proteins encoded by the RD1 region.

L7 ANSWER 10 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 10
AN 2003:153335 BIOSIS

DN PREV200300153335
TI Selecting the components for a safe and efficient **tuberculosis** subunit vaccine: Recent progress and post-genomic insights.
AU **Okkels, Limei Meng**; Doherty, T. Mark; Andersen, Peter [Reprint Author]
CS Department of Infectious Disease Immunology, Statens Serum Institut, 5 Artillerivej, DK-2300, Copenhagen, Denmark
pa@ssi.dk
SO Current Pharmaceutical Biotechnology, (February 2003) Vol. 4, No. 1, pp. 69-83. print.
ISSN: 1389-2010 (ISSN print).
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 19 Mar 2003
Last Updated on STN: 19 Mar 2003

L7 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:780953 CAPLUS
DN 135:343273
TI Cloning and immunogenicity of Mycobacterium **tuberculosis** proteins
IN Agger, Else Marie; Andersen, Peter; **Okkels, Li Mei Meng**; Weldingh, Karin
PA Statens Serum Institut, Den.
SO PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001079274	A2	20011025	WO 2001-DK276	20010419
	WO 2001079274	A3	20020711		
	WO 2001079274	B1	20020808		
	WO 2001079274	C1	20040429		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2405247	AA	20011025	CA 2001-2405247	20010419
	EP 1278769	A2	20030129	EP 2001-923542	20010419
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	DK 2000-666	A	20000419		
	DK 2001-283	A	20010221		
	WO 2001-DK276	W	20010419		

AB The authors disclose the identification and characterization of a number of novel Mycobacterium **tuberculosis** derived proteins and protein fragments. The proteins and protein fragments were examined for their ability to elicit interferon-γ production and/or a T-cell proliferative response in guinea pigs and humans with **tuberculosis**.

L7 ANSWER 12 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 11
AN 2001:302988 BIOSIS
DN PREV200100302988
TI Protection of mice with a **tuberculosis** subunit vaccine based on a fusion protein of antigen 85B and ESAT-6.
AU Olsen, Anja Weinreich; van Pinxteren, Laurens A. H.; **Okkels, Limei Meng**; Rasmussen, Peter Birk; Andersen, Peter [Reprint author]
CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5,

DK-2300, Copenhagen S, Denmark
pa@ssi.dk
SO Infection and Immunity, (May, 2001) Vol. 69, No. 5, pp. 2773-2778. print.
CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 27 Jun 2001
Last Updated on STN: 19 Feb 2002
AB In this study, we investigated the potential of a **tuberculosis** subunit vaccine based on fusion proteins of the immunodominant antigens ESAT-6 and antigen 85B. When the fusion proteins were administered to mice in the adjuvant combination dimethyl dioctadecylammonium bromide-monophosphoryl lipid A, a strong dose-dependent immune response was induced to both single components as well as to the fusion proteins. The immune response induced was accompanied by high levels of protective immunity and reached the level of Mycobacterium bovis BCG-induced protection over a broad dose range. The vaccine induced efficient immunological memory, which remained stable 30 weeks postvaccination.

L7 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:260319 CAPLUS
DN 132:292711
TI Tb vaccine and diagnostic based on antigens from the Mycobacterium **tuberculosis** cell
IN Andersen, Peter; Weldingh, Karin; Hansen, Christina Veggerby; Florio, Walter; **Okkels, Li Mei Meng**; Skjot, Rikke Louise Vinther; Rosenkrands, Ida
PA Statens Serum Institut, Den.
SO PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 10

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000021983	A2	20000420	WO 1999-DK538	19991008
WO 2000021983	A3	20001123		
W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2346218	AA	20000420	CA 1999-2346218	19991008
AU 9960784	A1	20000501	AU 1999-60784	19991008
AU 766093	B2	20031009		
EP 1117683	A2	20010725	EP 1999-947257	19991008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, IE, SI, LT, LV, FI, RO				
PRAI DK 1998-1281	A	19981008		
US 1999-116673P	P	19990121		
WO 1999-DK538	W	19991008		

AB The present invention relates to substantially pure polypeptides, which has a sequence identity of at least 80 % to an amino acid sequence disclosed, or which is a subsequence of at least 6 amino acids thereof, preferably a B- or T-cell epitope of the polypeptides disclosed. The polypeptide or the subsequence thereof has at least one of nine properties. The use of the disclosed polypeptides in medicine is disclosed, preferably as vaccine or diagnostic agents relating to virulent Mycobacterium. The invention further relates to the nucleotide sequences disclosed and the nucleotide sequences encoding the disclosed polypeptides. Medical and non-medical use of the nucleotide sequences is disclosed.

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=> e brock inger/au
E1            1     BROCK III T O/AU
E2            1     BROCK IINGER/AU
E3           27 --> BROCK INGER/AU
E4            2     BROCK IRVIN R/AU
E5            2     BROCK IV ROBERT C/AU
E6            1     BROCK IVAN H/AU
E7            1     BROCK IVAN HEINZ/AU
E8            1     BROCK IVAN R/AU
E9          943     BROCK J/AU
E10           1     BROCK J */AU
E11         360     BROCK J A/AU
E12           8     BROCK J A C/AU

=> s e3 and tuberculosis
L8           25 "BROCK INGER"/AU AND TUBERCULOSIS

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9           11 DUP REM L8 (14 DUPLICATES REMOVED)

=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 11 ANSWERS - CONTINUE? Y/(N):y

L9   ANSWER 1 OF 11  CAPLUS  COPYRIGHT 2005 ACS on STN DUPLICATE 1
AN   2004:59568  CAPLUS
DN   140:127185
TI   Antigens from Mycobacterium as vaccine and uses in tuberculosis
     diagnosis and treatment
IN   Andersen, Peter; Skjot, Rikke Louise Vinther; Okkels, Li Mei Meng;
     Brock, Inger; Oettinger, Thomas
PA   Den.
SO   U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 804,980.
     CODEN: USXXCO
DT   Patent
LA   English
FAN.CNT 10
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     --------------      ----   --------    -------------------    --------
PI   US 2004013685        A1    20040122    US 2001-872505         20010601
     EP 1449922           A2    20040825    EP 2004-76605          19980401
     EP 1449922           A3    20041117
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI, CY
     WO 2001004151        A2    20010118    WO 2000-DK398          20000713
     WO 2001004151        A3    20010712
         W:  AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
             CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI,
             GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
             KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX,
             MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM,
             TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,
             MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     US 2003147897        A1    20030807    US 2001-804980         20010313
PRAI DK 1997-1277         A     19971110
     US 1998-70488P       P     19980105
     US 1998-246191       B2    19981230
     DK 1999-1020         A     19990713
     US 1999-144011P      P     19990715
     US 2000-615947       A2    20000713
     WO 2000-DK398        A2    20000713
     US 2001-804980       A2    20010313
     DK 1993-798          A     19930702
     US 1993-123182       B2    19930920
     WO 1994-DK273        A2    19940701
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US 1995-465640 A1 19950605
DK 1997-376 A 19970402
US 1997-44624P P 19970418
EP 1998-913536 A3 19980401
US 1999-289388 B2 19990412

AB The present invention is based on the identification and characterization of 3 antigens, including Rv2653c, Rv2654c and RD1-ORF5, from Mycobacterium **tuberculosis**. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing **tuberculosis** caused by virulent mycobacteria in an animal, including a human being. The invention related to treating **tuberculosis** using antigens isolated from Mycobacterium **tuberculosis**.

L9 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:996402 CAPLUS
DN 141:423306
TI Compositions comprising multiple T cell epitopes of mycobacterial antigens for immunodiagnosis and immunotherapy of **tuberculosis**
IN Andersen, Peter; **Brock, Inger**; Weldingh, Karin
PA Statens Serum Institut, Den.
SO PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004099771	A1	20041118	WO 2004-DK314	20040506

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI DK 2003-699 A 20030508

AB The current used method for immunol. diagnosis of **tuberculosis** infection, the tuberculin skin test, is problematic for a number of reasons; it has low specificity in BCG vaccinated individuals, a high interobserver variance and requires skill to be read and interpreted. Furthermore it requires an extra visit to the clinic to have the test read. Both people vaccinated with BCG and those exposed to non-**tuberculosis** mycobacteria give a pos. skin test result similar to that seen in a TB infected individual. This also applies for purified protein derivative (PPD) when used in a blood cell based test. The present invention disclosed the development of an immunol. TB diagnostic tool based on a combination of T cell epitopes from proteins encoded by regions of the M. **tuberculosis** genome, that are not present in the BCG vaccine strain or in the most common non-**tuberculosis** mycobacteria. Four recently characterized proteins (i.e. Rv2654, Rv2653, Rv3873 and Rv3878) with this diagnostic potential were selected. Peptides from these proteins were tested one by one with peripheral blood mononuclear cells from microscopy or culture confirmed TB patients as well as from healthy BCG vaccinated controls. Some combinations of peptides showed a sensitivity level comparable to the level seen with these peptides combined with ESAT 6 and CFP 10 gave a sensitivity of 93% representing a raise in sensitivity of about 26-33% compared to using ESAT6 or CFP10 alone. The results from a panel of TB patients, using a collection of the new specific epitopes clearly demonstrates, the addition of other specific epitopes to the already known specific antigens, increases the sensitivity of a diagnostic assay based on cell mediated immune response.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 2
AN 2004:309660 BIOSIS
DN PREV200400309678
TI Healthy individuals that control a latent infection with Mycobacterium **tuberculosis** express high evels of Th1 cytokines and the IL-4 antagonist IL-4delta2.
AU Demissie, Abebech; Abebe, Markos; Aseffa, Abraham; Rook, Graham; Fletcher, Helen; Zumla, Alimuddin; Weldingh, Karin; **Brock, Inger**; Andersen, Peter; Doherty, T. Mark [Reprint Author]; VACSEL Study Group
CS Dept Infect Dis Immunol, Statens Serum Inst, Artillerivej 5, DK-2300, Copenhagen, S, Denmark
TMD@ssi.dk
SO Journal of Immunology, (June 1 2004) Vol. 172, No. 11, pp. 6938-6943. print.
ISSN: 0022-1767 (ISSN print).
DT Article
LA English
ED Entered STN: 7 Jul 2004
Last Updated on STN: 7 Jul 2004
AB The majority of healthy individuals exposed to Mycobacterium **tuberculosis** will not develop disease and identifying what constitutes "protective immunity" is one of the holy grails of M. **tuberculosis** immunology. It is known that IFN-gamma is essential for protection, but it is also apparent that IFN-gamma levels alone do not explain the immunity/susceptibility dichotomy. The controversy regarding correlates of immunity persists because identifying infected but healthy individuals (those who are immune) has been problematic. We have therefore used recognition of the M. **tuberculosis** virulence factor early secretory antigenic target 6 to identify healthy, but infected individuals from **tuberculosis** (TB)-endemic and nonendemic regions (Ethiopia and Denmark) and have compared signals for cytokines expressed directly ex vivo with the pattern found in TB patients. We find that TB patients are characterized by decreased levels of Th1 cytokines and increased levels of IL-10 compared with the healthy infected and noninfected community controls. Interestingly, the healthy infected subjects exhibited a selective increase of message for the IL-4 antagonist, IL-4delta2, compared with both TB patients or noninfected individuals. These data suggest that long-term control of M. **tuberculosis** infection is associated not just with elevated Th1 responses but also with inhibition of the Th2 response.

L9 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3
AN 2004:572566 CAPLUS
DN 141:294300
TI Specific T-cell epitopes for immunoassay-based diagnosis of Mycobacterium **tuberculosis** infection
AU **Brock, Inger**; Weldingh, Karin; Leyten, Eliane M. S.; Arend, Sandra M.; Ravn, Pernille; Andersen, Peter
CS Department of Infectious Disease Immunology, Statens Serum Institute, Copenhagen, Den.
SO Journal of Clinical Microbiology (2004), 42(6), 2379-2387
CODEN: JCMIDW; ISSN: 0095-1137
PB American Society for Microbiology
DT Journal
LA English
AB The currently used method for immunol. detection of **tuberculosis** infection, the tuberculin skin test, has low specificity. Antigens specific for Mycobacterium **tuberculosis** to replace purified protein derivative are therefore urgently needed. We have performed a rigorous assessment of the diagnostic potential of four recently identified antigens (Rv2653, Rv2654, Rv3873, and Rv3878) from genomic regions that are lacking from the Mycobacterium bovis bacillus Calmette-Guerin (BCG) vaccine strains as well as from the most common nontuberculous mycobacteria. The fine specificity of potential epitopes in these mols. was evaluated by sensitive testing of the T-cell responses

of peripheral blood mononuclear cells derived from M. bovis BCG-vaccinated healthy individuals to synthesized overlapping peptides. Three of the four mols. contained regions with significant specificity problems (Rv2653, Rv3873, and Rv3878). We selected and combined the specific peptide stretches from the four proteins not recognized by M. bovis BCG-vaccinated individuals. These peptide stretches were tested with peripheral blood mononuclear cells obtained from patients with microscopy-or culture-confirmed **tuberculosis** and from healthy M. bovis BCG-vaccinated controls. The combination of the most promising stretches from this anal. showed a sensitivity level (57%) comparable to the level found with the two well-known M. **tuberculosis**-specific proteins ESAT-6 and CFP-10 (75 and 66%, resp.). The combination of ESAT-6, CFP-10, and the novel specific peptide stretches gave an overall sensitivity of 84% at a specificity of 97%. In a validation experiment with new exptl. groups, the sensitivities obtained were 57% for the combination of peptides and 90% for the combination of the peptides, ESAT-6, and CFP-10. This combination gave a specificity of 95%.

RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 4
AN 2004:211482 BIOSIS
DN PREV200400213609
TI Mapping immune reactivity toward Rv2653 and Rv2654: Two novel low-molecular-mass antigens found specifically in the Mycobacterium **tuberculosis** complex.
AU Aagaard, Claus [Reprint Author]; **Brock, Inger**; Olsen, Anja; Ottenhoff, Tom H. M.; Weldingh, Karin; Andersen, Peter
CS Dept. of Infectious Disease Immunology, Statens Serum Institute, Artillerivej 5, DK-2300, Copenhagen, Denmark
caa@ssi.dk
SO Journal of Infectious Diseases, (1 March 2004) Vol. 189, No. 5, pp. 812-819. print.
CODEN: JIDIAQ. ISSN: 0022-1899.
DT Article
LA English
ED Entered STN: 14 Apr 2004
Last Updated on STN: 14 Apr 2004
AB New tools are urgently needed for the detection of latent **tuberculosis** (TB). We evaluated the diagnostic potential of 2 novel Mycobacterium **tuberculosis** complex-specific candidate antigens (Rv2653 and Rv2654) and investigated T cell recognition during natural infection in humans and experimental infection in guinea pigs. Peripheral blood mononuclear cells stimulated with peptide pools covering the full length of Rv2654 induced interferon-gamma release in 10 of 19 patients with TB. Neither Rv2654 single peptides nor Rv2654 pools were recognized by bacille Calmette-Guerin-vaccinated donors. However, peptides from Rv2653 were recognized by both patients group. The cross-reactive epitope(s) in Rv2653 were located in a 36-amino acid stretch in the center of the molecule. Rv2654 also induced M. **tuberculosis**-specific skin-test responses in 3 of 4 aerosol-infected guinea pigs. Rv2654 is a strongly recognized T cell antigen that is highly specific for TB and has potential as a novel cell-mediated immunity-based TB diagnostic agent.

L9 ANSWER 6 OF 11 MEDLINE on STN
AN 2004317793 MEDLINE
DN PubMed ID: 15087297
TI Comparison of tuberculin skin test and new specific blood test in **tuberculosis** contacts.
CM Comment in: Am J Respir Crit Care Med. 2004 Jul 1;170(1):5-6. PubMed ID: 15220119
AU **Brock Inger**; Weldingh Karin; Lillebaek Troels; Follmann Frank; Andersen Peter
CS Department of Infectious Disease Immunology, Statens Serum Institut, Artillerivej 5, DK-2300 Copenhagen S, Denmark.
SO American journal of respiratory and critical care medicine, (2004 Jul 1)

170 (1) 65-9. Electronic Publication: 2004-04-15.
Journal code: 9421642. ISSN: 1073-449X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200408
ED Entered STN: 20040629
Last Updated on STN: 20040806
Entered Medline: 20040805
AB The tuberculin skin test used to detect latent Mycobacterium **tuberculosis** infection has many drawbacks, and a new diagnostic test for latent **tuberculosis** (QuantiFERON-TB [QTF-TB]) has recently been introduced. This test measures the production of IFN-gamma in whole blood upon stimulation with purified protein derivative (PPD). The QTF-TB test addresses the operational problems with the tuberculin skin test, but, as the test is based on PPD, it still has a low specificity in populations vaccinated with the Bacille Calmette-Guerin (BCG) vaccine. We have modified the test to include the antigens ESAT-6 and CFP-10, which are not present in BCG vaccine strains or the vast majority of nontuberculous mycobacteria. This test was used to detect infection in contacts in a **tuberculosis** outbreak at a Danish high school. The majority of the contacts were BCG-unvaccinated, which allowed a direct comparison of the skin test and the novel blood test in individuals whose skin test was not confounded by vaccination. An excellent agreement between the two tests was found (94%, kappa value 0.866), and in contrast to the blood test based on PPD, the novel blood test was not influenced by the vaccination status of the subjects tested.

L9 ANSWER 7 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 5
AN 2004:33002 BIOSIS
DN PREV200400035432
TI PPE protein (Rv3873) from DNA segment RD1 of Mycobacterium **tuberculosis**: Strong recognition of both specific T-cell epitopes and epitopes conserved within the PPE family.
AU Okkels, Limei Meng [Reprint Author]; **Brock, Inger**; Follmann, Frank; Agger, Else Marie; Arend, Sandra M.; Ottenhoff, Tom H. M.; Oftung, Fredrik; Rosenkrands, Ida; Andersen, Peter
CS Department of Infectious Disease Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen, Denmark
lmo@ssi.dk
SO Infection and Immunity, (November 2003) Vol. 71, No. 11, pp. 6116-6123. print.
ISSN: 0019-9567 (ISSN print).
DT Article
LA English
ED Entered STN: 7 Jan 2004
Last Updated on STN: 7 Jan 2004
AB Proteins encoded by DNA segment RD1 of Mycobacterium **tuberculosis** have recently been demonstrated to play important roles in bacterial virulence, vaccine development, and diagnostic reagent design. Previously, we characterized two immunodominant T-cell antigens, the early secreted antigen target (ESAT-6),and the 10-kDa culture filtrate protein (CFP10), which are encoded by the esx-1hp operon in this region. In the present study we characterized a third putative open reading frame in this region, rv3873, which encodes a PPE protein. We found that the rv3873 gene is expressed in M. **tuberculosis** H37Rv and that the native protein, Rv3873, is predominantly associated with the mycobacterial cell or wall. When tested as a His-tagged recombinant protein, Rv3873 stimulated high levels of gamma interferon secretion in peripheral blood mononuclear cells isolated from **tuberculosis** (TB) patients, as well as from healthy tuberculin purified protein derivative-positive donors. In contrast to other RD1-encoded antigens, Rv3873 was also found to be recognized by a significant proportion of Mycobacterium bovis BCG-vaccinated donors. Epitope mapping performed with overlapping peptides revealed a broad pattern of T-cell recognition comprising both TB-specific epitopes and epitopes also recognized by BCG-vaccinated

donors. The immunodominant epitope (residues 118 to 1.35) for both TB patients and BCG-vaccinated individuals was found to be highly conserved among a large number of PPE family members.

L9 ANSWER 8 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 6
AN 2004:76163 BIOSIS
DN PREV200400078267
TI Human T-cell responses to the RD1-encoded protein TB27.4 (Rv3878) from Mycobacterium **tuberculosis**.
AU Agger, Else Marie [Reprint Author]; **Brock, Inger**; Okkels, Limei Meng; Arend, Sandra M.; Aagaard, Claus S.; Weldingh, Karin N.; Andersen, Peter
CS Department of Infectious Disease Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen, S, Denmark
eag@ssi.dk
SO Immunology, (December 2003) Vol. 110, No. 4, pp. 507-512. print.
CODEN: IMMUAM. ISSN: 0019-2805.
DT Article
LA English
ED Entered STN: 4 Feb 2004
Last Updated on STN: 4 Feb 2004
AB In recent years, there has been considerable focus on the discovery and characterization of proteins derived from Mycobacterium **tuberculosis** leading to the identification of a number of candidate antigens for use in vaccine development or for diagnostic purposes. Previous experiments have demonstrated an important immunological role for proteins encoded by the RD1 region, which is absent from all strains of bacillus Calmette-Guerin (BCG) but present in the genomes of virulent M. bovis and M. **tuberculosis**. Herein, we have studied human T-cell responses to the antigen encoded by the putative open reading frame (rv3878) of the RD1 region. Immunoblot analysis revealed that rv3878 was expressed and the native protein was designated TB27.4. Immunological evaluations demonstrate that TB27.4 elicits a prominent immune response in human **tuberculosis** patients with a dominant region in the C-terminal part of the molecule. In contrast, very limited responses were seen in M. bovis BCG-vaccinated donors. This study therefore emphasizes the diagnostic potential of proteins encoded by the RD1 region.

L9 ANSWER 9 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 7
AN 2002:559608 BIOSIS
DN PREV200200559608
TI Epitope mapping of the immunodominant antigen TB10.4 and the two homologous proteins TB10.3 and TB12.9, which constitute a subfamily of the esat-6 gene family.
AU Skjot, Rikke Louise Vinther; **Brock, Inger**; Arend, Sandra M.; Munk, Martin E.; Theisen, Michael; Ottenhoff, Tom H. M.; Andersen, Peter [Reprint author]
CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen S, Denmark
pa@ssi.dk
SO Infection and Immunity, (October, 2002) Vol. 70, No. 10, pp. 5446-5453. print.
CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 30 Oct 2002
Last Updated on STN: 30 Oct 2002
AB The human T-cell recognition of the low-molecular-mass culture filtrate antigen TB10.4 was evaluated in detail. The molecule was strongly recognized by T cells isolated from **tuberculosis** (TB) patients and from BCG-vaccinated donors. The epitopes on TB10.4 were mapped with overlapping peptides and found to be distributed throughout the molecule. The broadest response was found in TB patients, whereas the response in BCG-vaccinated donors was focused mainly toward a dominant epitope located in the N terminus (amino acids 1 to 18). The gene encoding TB10.4 was

found to belong to a subfamily within the esat-6 family that consists of the three highly homologous proteins TB10.4, TB10.3, and TB12.9 (Rv0288, Rv3019c, and Rv3017c, respectively). Southern blot analysis combined with database searches revealed that the three members of the TB10.4 family were present only in strains of the Mycobacterium **tuberculosis** complex, including BCG, and M. kansasii, whereas other atypical mycobacteria had either one (M. avium, M. intracellulare, and M. marinum) or none (M. scrofulaceum, M. fortuitum, and M. szulgai) of the genes. The fine specificity of the T-cell response to the three closely related esat-6 family members was markedly different, with only a few epitopes shared between the molecules. Minimal differences in the amino acid sequence translated into large differences in recognition by T cells and secretion of gamma interferon. In general, the peptides from TB10.4 stimulated the largest responses, but epitopes unique to both TB10.3 and TB12.9 were found. The relevance of the findings for TB vaccine development and as a potential mechanism for immune evasion is discussed.

L9 ANSWER 10 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2001:94979 BIOSIS
DN PREV200100094979
TI Use of ESAT-6 and CFP-10 antigens for diagnosis of extrapulmonary **tuberculosis**.
AU Munk, Martin E. [Reprint author]; Arend, Sandra M.; **Brock, Inger**; Ottenhoff, Tom H. M.; Andersen, Peter
CS Dept. of Tuberculosis Immunology, States Serum Institute, 5, Artillerivej, 2300, Copenhagen S, Denmark
mmn@ssi.dk
SO Journal of Infectious Diseases, (1 January, 2001) Vol. 183, No. 1, pp. 175-176. print.
CODEN: JIDIAQ. ISSN: 0022-1899.
DT Letter
LA English
ED Entered STN: 21 Feb 2001
Last Updated on STN: 15 Feb 2002

L9 ANSWER 11 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 8
AN 2000:104643 BIOSIS
DN PREV200000104643
TI Comparative evaluation of low-molecular-mass proteins from Mycobacterium **tuberculosis** identifies members of the ESAT-6 family as immunodominant T-cell antigens.
AU Skjot, Rikke Louise Vinther; Oettinger, Thomas; Rosenkrands, Ida; Ravn, Pernille; **Brock, Inger**; Jacobsen, Susanne; Andersen, Peter [Reprint author]
CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen S, Denmark
SO Infection and Immunity, (Jan., 2000) Vol. 68, No. 1, pp. 214-220. print.
CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 22 Mar 2000
Last Updated on STN: 3 Jan 2002
AB Culture filtrate from Mycobacterium **tuberculosis** contains protective antigens of relevance for the generation of a new antituberculosis vaccine. We have identified two previously uncharacterized M. **tuberculosis** proteins (TB7.3 and TB10.4) from the highly active low-mass fraction of culture filtrate. The molecules were characterized, mapped in a two-dimensional electrophoresis reference map of short-term culture filtrate, and compared with another recently identified low-mass protein, CFP10 (F. X. Berthet, P. B. Rasmussen, I. Rosenkrands, P. Andersen, and B. Gicquel. Microbiology 144:3195-3203, 1998), and the well-described ESAT-6 antigen. Genetic analyses demonstrated that TB10.4 as well as CFP10 belongs to the ESAT-6 family of low-mass proteins, whereas TB7.3 is a low-molecular-mass protein outside this family. The proteins were expressed in Escherichia coli, and their immunogenicity was tested in cultures of peripheral blood mononuclear

cells from human **tuberculosis** (TB) patients, Mycobacterium bovis BCG-vaccinated donors, and nonvaccinated donors. The two ESAT-6 family members, TB10.4 and CFP10, were very strongly recognized and induced gamma interferon release at the same level (CFP10) as or at an even higher level (TB10.4) than ESAT-6. The non-ESAT-6 family member, TB7.3, for comparison, was recognized at a much lower level. CFP10 was found to distinguish TB patients from BCG-vaccinated donors and is, together with ESAT-6, an interesting candidate for the diagnosis of TB. The striking immunodominance of antigens within the ESAT-6 family is discussed, and hypotheses are presented to explain this targeting of the immune response during TB infection.

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=> e oettinger thomas/au
E1            5     OETTINGER T P/AU
E2            2     OETTINGER TH/AU
E3           22 --> OETTINGER THOMAS/AU
E4            6     OETTINGER THOMAS P/AU
E5            7     OETTINGER U/AU
E6            2     OETTINGER ULRICH/AU
E7          171     OETTINGER W/AU
E8            1     OETTINGER W H/AU
E9            1     OETTINGER W K/AU
E10           2     OETTINGER W K E/AU
E11           1     OETTINGER W ROBERTO/AU
E12          67     OETTINGER WILLI/AU

=> s e1-e4 and tuberculosis
L10          24 ("OETTINGER T P"/AU OR "OETTINGER TH"/AU OR "OETTINGER THOMAS"/A
                U OR "OETTINGER THOMAS P"/AU) AND TUBERCULOSIS

=> dup rem l10
PROCESSING COMPLETED FOR L10
L11          13 DUP REM L10 (11 DUPLICATES REMOVED)

=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 13 ANSWERS - CONTINUE? Y/(N):y

L11  ANSWER 1 OF 13  CAPLUS  COPYRIGHT 2005 ACS on STN DUPLICATE 1
AN   2004:490265  CAPLUS
DN   141:52841
TI   Cloning and characterization of genes encoding culture filtrate antigens
     involved in protective immunity to M. tuberculosis, and use
     thereof as vaccines and in diagnosis
IN   Andersen, Peter; Skiot, Rikke; Oettinger, Thomas; Rasmussen,
     Peter Birk; Rosenkrands, Ida; Weldingh, Karin; Florio, Walter
PA   Den.
SO   U.S. Pat. Appl. Publ., 109 pp., Cont.-in-part of U.S. 6,641,814.
     CODEN: USXXCO
DT   Patent
LA   English
FAN.CNT 10
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
PI   US 2004115211        A1    20040617    US 2003-620246         20030715
     US 6641814           B1    20031104    US 1998-50739          19980330
     EP 1449922           A2    20040825    EP 2004-76605          19980401
     EP 1449922           A3    20041117
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI, CY
PRAI DK 1997-376          A     19970402
     US 1997-44624P       P     19970418
     DK 1997-1277         A     19971110
     US 1998-70488P       P     19980105
     US 1998-50739        A2    19980330
     DK 1998-1281         A     19981008
     EP 1998-913536       A3    19980401
AB   The present invention is based on the identification and characterization
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of a number of M. **tuberculosis** derived antigens, isolated from culture filtrates of T cells from memory immune mice by T cell epitope mapping. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, resp. These antigens are suitable for use in vaccines and in diagnosis of infections.

L11 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2
AN 2004:59568 CAPLUS
DN 140:127185
TI Antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment
IN Andersen, Peter; Skjot, Rikke Louise Vinther; Okkels, Li Mei Meng; Brock, Inger; **Oettinger, Thomas**
PA Den.
SO U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 804,980. CODEN: USXXCO
DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004013685	A1	20040122	US 2001-872505	20010601
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	WO 2001004151	A2	20010118	WO 2000-DK398	20000713
	WO 2001004151	A3	20010712		
	W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2003147897	A1	20030807	US 2001-804980	20010313
PRAI	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-246191	B2	19981230		
	DK 1999-1020	A	19990713		
	US 1999-144011P	P	19990715		
	US 2000-615947	A2	20000713		
	WO 2000-DK398	A2	20000713		
	US 2001-804980	A2	20010313		
	DK 1993-798	A	19930702		
	US 1993-123182	B2	19930920		
	WO 1994-DK273	A2	19940701		
	US 1995-465640	A1	19950605		
	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	EP 1998-913536	A3	19980401		
	US 1999-289388	B2	19990412		

AB The present invention is based on the identification and characterization of 3 antigens, including Rv2653c, Rv2654c and RD1-ORF5, from Mycobacterium **tuberculosis**. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing **tuberculosis** caused by virulent mycobacteria in an animal, including a human being. The invention related to treating **tuberculosis** using antigens isolated from Mycobacterium **tuberculosis**.

L11 ANSWER 3 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 3
AN 2004:5335 BIOSIS
DN PREV200400007544
TI Nucleic acids fragments and polypeptide fragments derived from M. **tuberculosis**.
AU Andersen, Peter [Inventor, Reprint Author]; Nielsen, Rikke [Inventor]; **Oettinger, Thomas** [Inventor]; Rasmussen, Peter Birk [Inventor]; Rosenkrands, Ida [Inventor]; Weldingh, Karin [Inventor]; Florio, Walter [Inventor]
CS Bronshoj, Denmark
ASSIGNEE: Statens Serum Institut, Copenhagen, Denmark
PI US 6641814 20031104
SO Official Gazette of the United States Patent and Trademark Office Patents, (Nov 4 2003) Vol. 1276, No. 1. http://www.uspto.gov/web/menu/patdata.html. e-file.
ISSN: 0098-1133 (ISSN print).
DT Patent
LA English
ED Entered STN: 17 Dec 2003
Last Updated on STN: 17 Dec 2003
AB The present invention is based on the identification and characterization of a number of M. **tuberculosis** derived novel proteins and protein fragments (SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171). The invention is directed to the polypeptides and immunologically active fragments thereof, the genes encoding them, immunological compositions such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, respectively.

L11 ANSWER 4 OF 13 USPATFULL on STN
AN 2002:178550 USPATFULL
TI Nucleic acid fragments and polypeptide fragments derived from M. **tuberculosis**
IN Andersen, Peter, Bronshoj, DENMARK
Nielsen, Rikke, Frederiksberg C, DENMARK
Oettinger, Thomas, Hellerup, DENMARK
Rasmussen, Peter Birk, Kobenhaven O, DENMARK
Rosenkrands, Ida, Kobenhaven O, DENMARK
Weldingh, Karin, Kobenhaven N, DENMARK
Florio, Walter, Frederiksberg C, DENMARK
PA STATENS SERUM INSTITUT (non-U.S. corporation)
PI US 2002094336 A1 20020718
AI US 2001-791171 A1 20010220 (9)
RLI Division of Ser. No. US 1998-50739, filed on 30 Mar 1998, PENDING
PRAI DK 1997-376 19970402
DK 1997-1277 19971110
US 1997-44624P 19970418 (60)
US 1998-70488P 19980105 (60)
DT Utility
FS APPLICATION
LREP FROMMER LAWRENCE & HAUG LLP, 745 FIFTH AVENUE, NEW YORK, NY, 10151
CLMN Number of Claims: 53
ECL Exemplary Claim: 1
DRWN 6 Drawing Page(s)
LN.CNT 6134
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is based on the identification and characterization of a number of M. **tuberculosis** derived novel proteins and protein fragments (SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171). The invention is directed to the polypeptides and immunologically active fragments thereof, the genes encoding them, immunological compositions

such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, respectively.

L11 ANSWER 5 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 4
AN 2001:222123 BIOSIS
DN PREV200100222123
TI Diagnostic skin test for **tuberculosis**.
AU Haslov, Kaare [Inventor]; Andersen, Ase Bengaard [Inventor]; **Oettinger, Thomas** [Inventor]
PI US 6120776 20000919
SO Official Gazette of the United States Patent and Trademark Office Patents, (Sep. 19, 2000) Vol. 1238, No. 3. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DT Patent
LA English
ED Entered STN: 9 May 2001
Last Updated on STN: 18 Feb 2002
AB Diagnostic methods capable of discriminating between cell mediated immunologic responses due to on the one hand active **tuberculosis** caused by bacteria belonging to the **tuberculosis** complex (Mycobacterium **tuberculosis**, Mycobacterium africanum and Mycobacterium bovis) and on the other hand vaccination with an immunogenic agent conferring immunity to **tuberculosis**. A diagnostic kit is also provided, comprising a polypeptide (e.g. MPT64) capable of eliciting a delayed type hypersensitivity reaction (Dth) in animals with active **tuberculosis**, but not in animals vaccinated against TB with an immunogenic agent (e.g. M. bovis BCG strain: Danish 1331). Also provided are polypeptide fragments comprising a T-cell epitope of MPT64 as well as nucleic acid fragments encoding these polypeptide fragments.

L11 ANSWER 6 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 5
AN 2000:104643 BIOSIS
DN PREV200000104643
TI Comparative evaluation of low-molecular-mass proteins from Mycobacterium **tuberculosis** identifies members of the ESAT-6 family as immunodominant T-cell antigens.
AU Skjot, Rikke Louise Vinther; **Oettinger, Thomas**; Rosenkrands, Ida; Ravn, Pernille; Brock, Inger; Jacobsen, Susanne; Andersen, Peter [Reprint author]
CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen S, Denmark
SO Infection and Immunity, (Jan., 2000) Vol. 68, No. 1, pp. 214-220. print.
CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 22 Mar 2000
Last Updated on STN: 3 Jan 2002
AB Culture filtrate from Mycobacterium **tuberculosis** contains protective antigens of relevance for the generation of a new antituberculosis vaccine. We have identified two previously uncharacterized M. **tuberculosis** proteins (TB7.3 and TB10.4) from the highly active low-mass fraction of culture filtrate. The molecules were characterized, mapped in a two-dimensional electrophoresis reference map of short-term culture filtrate, and compared with another recently identified low-mass protein, CFP10 (F. X. Berthet, P. B. Rasmussen, I. Rosenkrands, P. Andersen, and B. Gicquel. Microbiology 144:3195-3203, 1998), and the well-described ESAT-6 antigen. Genetic analyses demonstrated that TB10.4 as well as CFP10 belongs to the ESAT-6 family of low-mass proteins, whereas TB7.3 is a low-molecular-mass protein outside this family. The proteins were expressed in Escherichia coli, and their immunogenicity was tested in cultures of peripheral blood mononuclear cells from human **tuberculosis** (TB) patients, Mycobacterium bovis BCG-vaccinated donors, and nonvaccinated donors. The two ESAT-6 family members, TB10.4 and CFP10, were very strongly recognized and induced gamma

interferon release at the same level (CFP10) as or at an even higher level (TB10.4) than ESAT-6. The non-ESAT-6 family member, TB7.3, for comparison, was recognized at a much lower level. CFP10 was found to distinguish TB patients from BCG-vaccinated donors and is, together with ESAT-6, an interesting candidate for the diagnosis of TB. The striking immunodominance of antigens within the ESAT-6 family is discussed, and hypotheses are presented to explain this targeting of the immune response during TB infection.

L11 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:684968 CAPLUS
DN 129:300060
TI Novel antigens of Mycobacterium **tuberculosis** culture filtrates and the genes encoding and their diagnostic and prophylactic use
IN Andersen, Peter; Nielsen, Rikke; Rosenkrands, Ida; Weldingh, Karin; Rasmussen, Peter Birk; **Oettinger, Thomas**; Florio, Walter
PA Statens Serum Institut, Den.
SO PCT Int. Appl., 264 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9844119	A1	19981008	WO 1998-DK132	19980401
	W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2285625	AA	19981008	CA 1998-2285625	19980401
	AU 9868204	A1	19981022	AU 1998-68204	19980401
	AU 740545	B2	20011108		
	EP 972045	A1	20000119	EP 1998-913536	19980401
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001515359	T2	20010918	JP 1998-541074	19980401
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	CA 2319380	AA	19990520	CA 1998-2319380	19981008
	WO 9924577	A1	19990520	WO 1998-DK438	19981008
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1029053	A1	20000823	EP 1998-947412	19981008
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	NZ 504951	A	20010629	NZ 1998-504951	19981008
	AU 750173	B2	20020711	AU 1998-94338	19981008
	EP 1484405	A1	20041208	EP 2004-77071	19981008
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PRAI	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	EP 1998-913536	A3	19980401		

WO 1998-DK132 W 19980401
EP 1998-947412 A3 19981008
WO 1998-DK438 W 19981008

AB Culture filtrate antigens of Mycobacterium **tuberculosis** are characterized and cDNAs encoding them are cloned. Some of the proteins are antigenic and suitable for use in vaccines and in diagnosis of infections, e.g. skin tests. A fusion protein of two of these antigens is a superior immunogen compared to the unfused proteins. Individual antigens from culture filtrates were identified by T cell mapping using T cells from memory immune mice. Genes for individual antigens were then cloned by screening a λgt11 expression vector with monoclonal antibodies. Manufacture of individual antigens with hexahistidine affinity labels is described.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 6
AN 1998:348514 BIOSIS
DN PREV199800348514
TI Delayed-type hypersensitivity responses to ESAT-6 and MPT64 from Mycobacterium **tuberculosis** in the guinea pig.
AU Elhay, Martin J.; **Oettinger, Thomas**; Andersen, Peter [Reprint author]
CS Dep. T.B. Immunol., Statens Serum Inst., Artillerivej 5, Copenhagen 2300, Denmark
SO Infection and Immunity, (July, 1998) Vol. 66, No. 7, pp. 3454-3456. print.
CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 13 Aug 1998
Last Updated on STN: 13 Aug 1998
AB Two antigens from Mycobacterium **tuberculosis**, ESAT-6 and MPT64, elicited delayed-type hypersensitivity (DTH) skin responses in outbred guinea pigs infected with M. **tuberculosis** by the aerosol and intravenous routes but not those sensitized with M. bovis BCG or M. avium. The DTH epitope of ESAT-6 was mapped to the C terminus. Nonresponders to the individual antigens were found, but all animals responded to a combination of ESAT-6 and MPT64 or their respective minimal target peptides. Correspondingly, these molecules could form the basis of a new skin test for **tuberculosis**.

L11 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:632476 CAPLUS
DN 125:325659
TI Key epitopes on the ESAT-6 antigen recognized in mice during the recall of protective immunity to Mycobacterium **tuberculosis**
AU Brandt, Lise; **Oettinger, Thomas**; Holm, Arne; Andersen, Aase B.; Andersen, Peter
CS Bacterial Vaccine and Mycobacteria Dep., Royal Veterinary and Agricultural Univ., Copenhagen, Den.
SO Journal of Immunology (1996), 157(8), 3527-3533
CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB The recall of long-lived immunity in a mouse model of **tuberculosis** (TB) is defined as an accelerated accumulation of reactive T cells in the target organs. The authors have recently identified antigen (Ag) 85B and a 6-kDa early secretory antigenic target, designated ESAT-6, as key antigenic targets recognized by these cells. Here, preferential recognition of the ESAT-6 Ag during the recall of immunity was shared by 5 of 6 genetically different strains of mice. Overlapping peptides spanning the sequence of ESAT-6 were used to map 2 T cell epitopes on this mol. One epitope recognized in the context of H-2b,d was located in the N-terminal part of the mol., whereas an epitope recognized in the context of H-2a,k covered amino acids 51-60. Shorter versions of the N-terminal epitope allowed the precise definition of a 13-amino acid core sequence

recognized in the context of H-2b. The peptide covering the N-terminal epitope was immunogenic, and a T cell response with the same fine specificity as that induced during TB infection was generated by immunization with the peptide in IFA. In the C57BL/6j strain, this single epitope was recognized by an exceedingly high frequency of splenic T cells (.apprx.1:1000), representing 25-35% of the total culture filtrate-reactive T cells recruited to the site of infection during the first phase of the recall response. These findings emphasize the relevance of this Ag in the immune response to TB and suggest that immunol. recognition in the first phase of infection is a highly restricted event dominated by a limited number of T cell clones.

L11 ANSWER 10 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 7
AN 1996:76919 BIOSIS
DN PREV199698649054
TI Evidence for occurrence of the ESAT-6 protein in Mycobacterium **tuberculosis** and virulent Mycobacterium bovis and for its absence in Mycobacterium bovis BCG.
AU Harboe, Morten [Reprint author]; **Oettinger, Thomas**; Wiker, Harald Gotten; Rosenkrands, Ida; Andersen, Peter
CS Inst. Immunol. Rheumatol., Univ. Oslo, N-0172 Oslo, Norway
SO Infection and Immunity, (1996) Vol. 64, No. 1, pp. 16-22.
CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 27 Feb 1996
Last Updated on STN: 27 Feb 1996
AB ESAT-6 is a secreted protein present in the short-term culture filtrate of Mycobacterium **tuberculosis** after growth on a synthetic Sauton medium. ESAT-6 has recently been demonstrated to induce strong T-cell responses in a mouse model of memory immunity after infection with M. **tuberculosis**. In Western blotting (immunoblotting), the monoclonal antibody HYB76-8. reacting with ESAT-6, gave a 6-kDa band in culture filtrates from M. **tuberculosis** and virulent Mycobacterium bovis. A distinct band in the 24-kDa region was observed in filtrates from four of eight substrains of M. bovis BCG that produced high levels of MPB64, while no band occurred in the 6-kDa region with any of these BCG substrains. Southern blotting and PCR experiments with genomic mycobacterial DNA showed the presence of the esat-6 gene in reference strains and clinical isolates of V. **tuberculosis** as well as in virulent M. bovis. The esat-6 gene could not be demonstrated in any of the eight substrains of M. bovis BCG tested by these techniques. Two gene deletions that distinguish M. bovis BCG from virulently M. bovis have thus now been demonstrated. Deletion of mpb64 affects four of the eight substrains tested; deletion of esat-6 affects all of them. The reaction of HYB76-8 at 26 kDa with four of the BCG substrains was demonstrated to result from cross-reactivity with MPB64. HYB76-8 was also shown to cross-react with the A, B, and C components of the antigen 85 complex and MPT51.

L11 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:498385 CAPLUS
DN 122:260539
TI Diagnostic skin test for **tuberculosis**: a method able to distinguish infection from vaccination
IN Hasloev, Kaare; Andersen, Aase Bengaard; **Oettinger, Thomas**
PA Statens Seruminstitut, Den.
SO PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9501440	A1	19950112	WO 1994-DK270	19940630

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, CZ, DE, DE, DK, DK, ES, FI, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LU, LV, MD,

MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, SK, TJ, TT, UA
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

	AU 9470686	A1	19950124	AU 1994-70686	19940630
	AU 685133	B2	19980115		
	EP 749486	A1	19961227	EP 1994-919572	19940630
	R: BE, CH, DE, ES, FR, GB, IT, LI				
	US 6120776	A	20000919	US 1996-569221	19960212
PRAI	DK 1993-797	A	19930702		
	WO 1994-DK270	W	19940630		

AB Diagnostic methods capable of discriminating between cell mediated immunol. responses due to on the one hand active **tuberculosis** caused by bacteria belonging to the **tuberculosis** complex (Mycobacterium **tuberculosis**, Mycobacterium africanum and Mycobacterium bovis) and on the other hand vaccination with an immunogenic agent conferring immunity to **tuberculosis**. A diagnostic kit is also provided, comprising a polypeptide (e.g. MPT64) capable of eliciting a delayed type hypersensitivity reaction in animals with active **tuberculosis**, but not in animals vaccinated against TB with an immunogenic agent (e.g. M. bovis BCG strain: Danish 1331). Also provided are polypeptide fragments comprising a T-cell epitope of MPT64 as well as nucleic acid fragments encoding these polypeptide fragments.

L11 ANSWER 12 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 8
AN 1996:21932 BIOSIS
DN PREV199698594067
TI Mapping of the delayed-type hypersensitivity-inducing epitope of secreted protein MPT64 from Mycobacterium **tuberculosis**.
AU **Oettinger, Thomas** [Reprint author]; Holm, Arne; Mtoni, Isaac M.; Andersen, Ase B.; Haslov, Kaare
CS Mycobacteria Dep., Div. Diagnostics, Statens Seruminstitut, Artillerivej 5, DK-2300 Copenhagen S, Denmark
SO Infection and Immunity, (1995) Vol. 63, No. 12, pp. 4613-4618. CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 12 Jan 1996
Last Updated on STN: 12 Jan 1996
AB The gene encoding the immunogenic protein MPT64 found in culture filtrates of Mycobacterium **tuberculosis** H37Rv was expressed in Escherichia coli K-12 and purified as a recombinant protein. The purified recombinant MPT64 elicited delayed-type hypersensitivity (DTH) in outbred guinea pigs sensitized with Mycobacterium bovis BCG Tokyo. The skin reactions were comparable to those obtained with native MPT64. No skin reactions were observed when either recombinant MPT64 or native MPT64 was used in guinea pigs sensitized with M. bovis BCG Danish 1331. Amino- and carboxy-terminal deletion mutants of MPT64 were purified as fusion proteins for the mapping of DTH-inducing epitopes on recombinant MPT64 by use of the guinea pig skin test model. The part of the molecule responsible for the biological activity was located at the carboxy-terminal end. Further studies with overlapping synthetic peptides have pinpointed the biological activity at a single DTH-inducing epitope consisting of 15 residues between amino acids Gly-173 and Ala-187. Screening by PCR of 56 clinical isolates of M. **tuberculosis** from Danish and Tanzanian patients demonstrated the presence of mpt64 in all of the strains. These results point to MPT64 as a possible candidate for a skin test reagent specific for diagnosis of human **tuberculosis**.

L11 ANSWER 13 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 9
AN 1994:271662 BIOSIS
DN PREV199497284662
TI Cloning and B-cell-epitope mapping of MPT64 from Mycobacterium **tuberculosis** H37Rv.
AU **Oettinger, Thomas** [Reprint author]; Andersen, Ase B.
CS Mycobacteria Dep., Sector Biotechnol., Statens Seruminstitut, Artillerivej

5, DK-2300 Copenhagen S, Denmark
SO Infection and Immunity, (1994) Vol. 62, No. 5, pp. 2058-2064.
CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
OS EMBL-X75361
ED Entered STN: 24 Jun 1994
Last Updated on STN: 24 Jun 1994
AB The gene of the immunogenic protein MPT64 found in culture filtrates of Mycobacterium **tuberculosis** H37Rv was cloned and sequenced. A comparison showed mpt64 and the gene encoding MPB64 from Mycobacterium bovis BCG Tokyo to be identical except for one silent mutation. The regions encoding the promoter and the signal peptide were also well conserved for the two sequences. Southern blot experiments on genomic mycobacterial DNA showed the presence of mpt64 in the M. **tuberculosis** substrains H37Rv, H37Ra, and Erdman and in the M. bovis BCG substrains Tokyo, Moreau, and Russian, whereas the M. bovis BCG substrains Glaxo, Pasteur, Canadian, Tice, and Danish 1331 and Mycobacterium leprae lack the gene. Southern blot analyses revealed differences in the restriction enzyme patterns within the M. **tuberculosis** substrains as well as within the M. bovis BCG substrains, indicating either different chromosomal localization of mpt64 or that mutations have occurred at different locations on the chromosomes. N-terminal and C-terminal deletion mutants were constructed for the mapping of B-cell epitopes on MPT64 with five monoclonal antibodies, C24b1, C24b2, C24b3, L24b4, and L24b5. Western blot (immunoblot) analysis revealed that the murine antibodies bind to one linear and three conformational epitopes.

=> s tuberculosis and (RD1-ORF5)
L12 14 TUBERCULOSIS AND (RD1-ORF5)

=> dup rem l12
PROCESSING COMPLETED FOR L12
L13 10 DUP REM L12 (4 DUPLICATES REMOVED)

=> d bib ab kwic 1-
YOU HAVE REQUESTED DATA FROM 10 ANSWERS - CONTINUE? Y/(N):y

L13 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1
AN 2004:490265 CAPLUS
DN 141:52841
TI Cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis
IN Andersen, Peter; Skiot, Rikke; Oettinger, Thomas; Rasmussen, Peter Birk; Rosenkrands, Ida; Weldingh, Karin; Florio, Walter
PA Den.
SO U.S. Pat. Appl. Publ., 109 pp., Cont.-in-part of U.S. 6,641,814.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004115211	A1	20040617	US 2003-620246	20030715
	US 6641814	B1	20031104	US 1998-50739	19980330
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PRAI	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-50739	A2	19980330		

DK 1998-1281 A 19981008
EP 1998-913536 A3 19980401

AB The present invention is based on the identification and characterization of a number of M. **tuberculosis** derived antigens, isolated from culture filtrates of T cells from memory immune mice by T cell epitope mapping. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, resp. These antigens are suitable for use in vaccines and in diagnosis of infections.

TI Cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis

AB The present invention is based on the identification and characterization of a number of M. **tuberculosis** derived antigens, isolated from culture filtrates of T cells from memory immune mice by T cell epitope mapping. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, resp. These antigens are suitable for use in vaccines and in diagnosis of infections.

ST sequence Mycobacterium culture filtrate antigen gene; **tuberculosis** vaccine diagnosis Mycobacterium culture filtrate antigen gene

IT 213992-10-0P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(M. **tuberculosis** culture filtrate antigen CFP29 N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-97-4P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(M. **tuberculosis** culture filtrate antigen CFP30A N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 213992-24-6P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(M. **tuberculosis** culture filtrate antigen CFP30B N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 213992-20-2P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(M. **tuberculosis** culture filtrate antigen CFP50 N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 213992-21-3P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(M. **tuberculosis** culture filtrate antigen CFP7B N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 213992-11-1P

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(M. **tuberculosis** culture filtrate antigen CFPSA N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-89-4P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(M. **tuberculosis** culture filtrate antigen CFPSB N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 213992-13-3P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(M. **tuberculosis** culture filtrate antigen CWP32 N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-88-3P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-23-6 706035-25-8 706035-27-0 706035-29-2 706035-31-6
706035-33-8 706035-35-0 706035-37-2 706035-39-4 706035-41-8
706035-43-0 706035-45-2 706035-47-4 706035-49-6 706035-51-0
706035-53-2 706035-55-4 706035-57-6 706035-59-8 706035-61-2
706035-63-4 706035-65-6 706035-67-8 706035-69-0 706035-71-4
706035-73-6 706035-75-8 706035-77-0 706035-79-2 706035-81-6
706035-83-8 706035-85-0
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-87-2
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-22-5 706035-24-7 706035-26-9 706035-28-1 706035-30-5
706035-32-7 706035-34-9 706035-36-1 706035-38-3 706035-40-7
706035-42-9 706035-44-1 706035-46-3 706035-48-5 706035-50-9
706035-52-1 706035-54-3 706035-56-5 706035-58-7 706035-60-1
706035-62-3 706035-64-5 706035-66-7 706035-68-9 706035-70-3
706035-72-5 706035-74-7 706035-76-9 706035-78-1 706035-80-5
706035-82-7 706035-84-9
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-86-1
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706036-03-5 706036-04-6 706036-05-7 706036-06-8 706036-07-9
706036-08-0 706036-09-1 706036-10-4 706036-11-5 706036-12-6

706036-13-7 706036-14-8 706036-15-9 706036-16-0 706036-17-1
706036-18-2 706036-19-3 706036-20-6 706036-21-7 706036-22-8
706036-23-9 706036-24-0 706036-25-1 706036-26-2 706036-27-3
706036-28-4 706036-29-5 706036-30-8 706036-31-9 706036-32-0
706036-33-1 706036-34-2 706036-35-3 706036-36-4 706036-37-5
706036-38-6 706036-39-7 706036-40-0 706036-41-1 706036-42-2
706036-43-3 706036-44-4 706036-45-5 706036-46-6 706036-47-7
706036-48-8 706036-49-9 706036-50-2 706036-51-3 706036-52-4
706036-53-5 706036-54-6 706036-55-7 706036-58-0 706036-59-1
706036-60-4 706036-61-5 706036-62-6 706036-63-7 706036-64-8
706036-65-9 706036-66-0 706036-67-1 706036-68-2 706036-69-3
706036-70-6 706036-71-7 706036-72-8 706036-73-9 706036-74-0
706036-75-1 706036-76-2 706036-77-3 706036-78-4 706036-79-5
RL: PRP (Properties)
(unclaimed nucleotide sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706036-56-8 706036-57-9 706036-80-8 706036-81-9
RL: PRP (Properties)
(unclaimed protein sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as v

SYSTEM LIMITS
EXCEEDED

L13 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2
AN 2004:59568 CAPLUS
DN 140:127185
TI Antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment
IN Andersen, Peter; Skjot, Rikke Louise Vinther; Okkels, Li Mei Meng; Brock, Inger; Oettinger, Thomas
PA Den.
SO U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 804,980.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004013685	A1	20040122	US 2001-872505	20010601
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	WO 2001004151	A2	20010118	WO 2000-DK398	20000713
	WO 2001004151	A3	20010712		
	W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2003147897	A1	20030807	US 2001-804980	20010313
PRAI	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-246191	B2	19981230		
	DK 1999-1020	A	19990713		
	US 1999-144011P	P	19990715		
	US 2000-615947	A2	20000713		
	WO 2000-DK398	A2	20000713		
	US 2001-804980	A2	20010313		

DK 1993-798	A	19930702
US 1993-123182	B2	19930920
WO 1994-DK273	A2	19940701
US 1995-465640	A1	19950605
DK 1997-376	A	19970402
US 1997-44624P	P	19970418
EP 1998-913536	A3	19980401
US 1999-289388	B2	19990412

AB The present invention is based on the identification and characterization of 3 antigens, including Rv2653c, Rv2654c and **RD1-ORF5**, from Mycobacterium **tuberculosis**. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing **tuberculosis** caused by virulent mycobacteria in an animal, including a human being. The invention related to treating **tuberculosis** using antigens isolated from Mycobacterium **tuberculosis**.

TI Antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment

AB The present invention is based on the identification and characterization of 3 antigens, including Rv2653c, Rv2654c and **RD1-ORF5**, from Mycobacterium **tuberculosis**. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing **tuberculosis** caused by virulent mycobacteria in an animal, including a human being. The invention related to treating **tuberculosis** using antigens isolated from Mycobacterium **tuberculosis**.

ST Mycobacterium antigen vaccine **tuberculosis** diagnosis

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**RD1-ORF5**; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Rv2653c; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Rv2654c; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT Mycobacterium bovis
(antigen **RD1-ORF5** expressed in; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antibodies and Immunoglobulins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT Fusion proteins (chimeric proteins)
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antigens in; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT Animal
Human
(diagnosis of **tuberculosis** in; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT **Tuberculosis**
(diagnosis, **tuberculosis**; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT Diagnosis
(immunodiagnosis; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)
IT Drug delivery systems
(injections, intradermally; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)
IT Antibodies and Immunoglobulins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(monoclonal; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)
IT Epitopes
Molecular cloning
Mycobacterium **tuberculosis**
Tuberculosis
Tuberculostatics
Vaccines
(protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)
IT Immunoassay
(skin test; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)
IT Diagnosis
(**tuberculosis**, **tuberculosis**; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)
IT Immunization
(vaccination; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)
IT Mycobacterium
(virulent; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)
IT Interferons
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(γ; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)
IT 649655-13-0 649655-14-1 649655-15-2 649655-16-3 649655-17-4
649655-18-5 649655-19-6 649655-20-9
RL: PRP (Properties)
(unclaimed nucleotide sequence; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)
IT 649655-09-4 649655-10-7 649655-11-8 649655-12-9
RL: PRP (Properties)
(unclaimed protein sequence; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)
IT 649543-98-6 649544-02-5 649544-05-8 649544-08-1 649544-11-6
649544-14-9 649544-18-3 649544-21-8 649544-24-1 649544-27-4
649544-30-9 649544-33-2 649544-36-5 649544-40-1 649544-43-4
649544-46-7 649544-49-0 649544-52-5 649544-55-8 649544-58-1
649544-61-6 649544-65-0 649544-68-3 649544-71-8 649544-74-1
649544-79-6 649544-82-1 649544-85-4 649544-88-7 649544-91-2
649544-94-5 649544-97-8 649545-00-6 649545-03-9 649545-06-2
649545-09-5 649545-12-0 649545-15-3 649545-18-6 649545-21-1
649545-24-4 649545-27-7 649545-30-2 649545-33-5 649545-36-8
649545-39-1 649545-42-6 649545-45-9 649545-48-2 649545-51-7
649545-54-0 649545-57-3 649655-21-0 649655-22-1 649655-23-2
649655-24-3 649655-25-4 649655-26-5 649655-27-6 649655-28-7
649655-29-8 649655-30-1
RL: PRP (Properties)
(unclaimed sequence; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)

L13 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:60336 CAPLUS
DN 140:144681
TI Mycobacterium low oxygen-induced antigens and genes for vaccines or diagnostics of **tuberculosis**

IN Andersen, Peter; Rosenkrands, Ida; Stryhn, Anette
PA Statens Serum Institut, Den.
SO PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004006952	A2	20040122	WO 2003-DK477	20030708
	WO 2004006952	A3	20040318		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1523331	A2	20050420	EP 2003-763613	20030708
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 2004057963	A1	20040325	US 2003-617038	20030711
PRAI	DK 2002-1098	A	20020713		
	US 2002-401725P	P	20020807		
	WO 2003-DK477	W	20030708		

AB The present invention is based on a number of M. **tuberculosis** derived proteins and protein fragments which are induced during the latent stage of infection characterized by low oxygen tension in the microenvironment of the infecting TB-bacteria. The invention is directed to the use of these polypeptides, immunol. active fragments thereof and the genes encoding them for immunol. compns. such as therapeutic vaccines and diagnostic reagents.

TI Mycobacterium low oxygen-induced antigens and genes for vaccines or diagnostics of **tuberculosis**

AB The present invention is based on a number of M. **tuberculosis** derived proteins and protein fragments which are induced during the latent stage of infection characterized by low oxygen tension in the microenvironment of the infecting TB-bacteria. The invention is directed to the use of these polypeptides, immunol. active fragments thereof and the genes encoding them for immunol. compns. such as therapeutic vaccines and diagnostic reagents.

ST Mycobacterium **tuberculosis** low oxygen induced antigen gene vaccine diagnostic

; BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(γ; Mycobacterium low oxygen-induced antigens and genes for vaccines or diagnostics of **tuberculosis**)

IT 650674-04-7P 650674-05-8P 650674-06-9P 650674-07-0P 650674-08-1P
650674-09-2P 650674-10-5P 650674-11-6P 650674-12-7P 650674-13-8P
650674-14-9P 650674-15-0P 650674-16-1P 650674-17-2P 650674-18-3P
650674-19-4P 650674-20-7P 650674-21-8P 650674-22-9P 650674-23-0P
650674-24-1P 650674-25-2P 650674-26-3P 650674-27-4P 650674-28-5P
650674-29-6P 650674-30-9P 650674-31-0P 650674-32-1P 650674-33-2P
650674-34-3P 650674-35-4P 650674-36-5P 650674-37-6P 650674-38-7P
650674-39-8P 650674-40-1P 650674-41-2P 650674-42-3P 650674-43-4P
650674-44-5P 650674-45-6P 650674-46-7P 650674-47-8P 650674-48-9P
651361-06-7P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; Mycobacterium low oxygen-induced antigens and genes for vaccines or diagnostics of **tuberculosis**)

IT 7782-44-7, Oxygen, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(low; Mycobacterium low oxygen-induced antigens and genes for vaccines

or diagnostics of **tuberculosis**)

IT 650674-49-0P 650674-50-3P 650674-51-4P 650674-52-5P 650674-53-6P
650674-54-7P 650674-55-8P 650674-56-9P 650674-57-0P 650674-58-1P
650674-59-2P 650674-60-5P 650674-61-6P 650674-62-7P 650674-63-8P
650674-64-9P 650674-65-0P 650674-66-1P 650674-67-2P 650674-68-3P
650674-69-4P 650674-70-7P 650674-71-8P 650674-72-9P 650674-73-0P
650674-74-1P 650674-75-2P 650674-76-3P 650674-77-4P 650674-78-5P
650674-79-6P 650674-80-9P 650674-81-0P 650674-82-1P 650674-83-2P
650674-84-3P 650674-85-4P 650674-86-5P 650674-87-6P 650674-88-7P
650674-89-8P 650674-90-1P 650674-91-2P 650674-92-3P 650674-93-4P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; Mycobacterium low oxygen-induced antigens and genes for vaccines or diagnostics of **tuberculosis**)

IT 650674-94-5 650674-95-6 650674-96-7 650674-97-8 650674-98-9
650674-99-0 650675-00-6 650675-01-7 650675-02-8 650675-03-9
650675-04-0 650675-05-1 650675-06-2 650675-07-3 650675-08-4
650675-09-5 650675-10-8 650675-11-9 650675-12-0 650675-13-1
650675-14-2 650675-15-3 650675-16-4 650675-17-5 650675-18-6
650675-19-7 650675-20-0 650675-21-1 650675-22-2 650675-23-3
650675-24-4 650675-25-5 650675-26-6 650675-27-7 650675-28-8
650675-29-9 650675-30-2 650675-31-3 650675-32-4 650675-33-5
650675-34-6 650675-35-7 650675-36-8 650675-37-9 650675-38-0
650675-39-1 650675-40-4 650675-41-5 650675-42-6 650675-43-7
650675-44-8 650675-45-9 650675-46-0 650675-47-1 650675-48-2
650675-49-3 650675-50-6 650675-51-7 650675-52-8 650675-53-9
650675-54-0 650675-55-1 650675-56-2 650675-57-3 650675-58-4
650675-59-5 650675-60-8 650675-61-9 650675-62-0 650675-63-1
650675-64-2 650675-65-3 650675-66-4 650675-67-5 650675-68-6
650675-69-7 650675-70-0 650675-71-1 650675-72-2 650675-73-3
650675-74-4 650675-75-5 650675-76-6 650675-77-7 650675-78-8
650675-79-9 650675-80-2 650675-81-3 650675-82-4 650675-83-5
650675-84-6 650675-85-7
RL: PRP (Properties)
(unclaimed sequence; mycobacterium low oxygen-induced antigens and genes for vaccines or diagnostics o

SYSTEM LIMITS EXCEEDED

L13 ANSWER 4 OF 10 USPATFULL on STN
AN 2004:76186 USPATFULL
TI Therapeutic TB vaccine
IN Andersen, Peter, Bronshoj, DENMARK
Rosenkrands, Ida, Vaerlose, DENMARK
Stryhn, Anette, Virum, DENMARK
PI US 2004057963 A1 20040325
AI US 2003-617038 A1 20030711 (10)
PRAI DK 2002-1098 20020713
US 2002-401725P 20020807 (60)
DT Utility
FS APPLICATION
LREP HOWSON AND HOWSON, ONE SPRING HOUSE CORPORATION CENTER, BOX 457, 321 NORRISTOWN ROAD, SPRING HOUSE, PA, 19477
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN 7 Drawing Page(s)
LN.CNT 6018
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Therapeutic vaccines comprising polypeptides expressed during the latent stage of mycobacteria infection are provided, as are multiphase vaccines, and methods for treating and preventing **tuberculosis**
.
AB . . . expressed during the latent stage of mycobacteria infection are provided, as are multiphase vaccines, and methods for treating and preventing **tuberculosis**.
SUMM [0002] The present invention discloses a therapeutic vaccine against latent or active **tuberculosis** infection caused by the

tuberculosis complex microorganisms (Mycobacterium **tuberculosis**., M.bovis, M.africanum). The invention furthermore discloses a multi-phase vaccine that can be administered either prophylactically or therapeutically as well as a diagnostic reagent for the detection of latent stages of **tuberculosis**.

SUMM [0003] Human **tuberculosis** caused by Mycobacterium **tuberculosis** (M. **tuberculosis**) is a severe global health problem, responsible for approx. 3 million deaths annually, according to the WHO. The worldwide incidence of new **tuberculosis** (TB) cases had been falling during the 1960s and 1970s but during recent decades this trend has markedly changed in part due to the advent of AIDS and the appearance of multidrug resistant strains of M. **tuberculosis**.

SUMM [0004] Organisms of the **tuberculosis** complex can cause a variety of diseases, but the commonest route of invasion is by inhalation of bacteria. This initiates. . . for the rest of their life. Certainly, individuals who have been healthy for years or even decades can suddenly develop **tuberculosis**, which has proven to be caused by the same organism they were infected with many years previously. M. **tuberculosis** and other organisms of the TB complex are unique in that the mycobacteria can evade the immune response and survive. . .

SUMM [0005] The course of a M. **tuberculosis** infection runs essentially through 3 phases, as illustrated in FIG. 1. During the acute phase, the bacteria proliferate in the. . . a latent phase is established where the bacterial load is kept stable at a low level. In this phase M. **tuberculosis** goes from active multiplication to dormancy, essentially becoming non-replicating and remaining inside the granuloma. In some cases, the infection goes. . .

SUMM [0009] It has been suggested that the transition of M. **tuberculosis** from primary infection to latency is accompanied by changes in gene expression (see, for example, Honer zu Bentrup, 2001, which. . .

SUMM . . . candidate. The only way to determine if a protein is recognized by the immune system during latent infection with M. **tuberculosis** is to produce the given protein and test it in an appropriate assay as described herein. Of the more than. . .

DRWD . . . the infection. For analysis of therapeutic vaccinations a reactivation model is established, where aerosol infected mice are treated with anti-M **tuberculosis** drugs for 8 weeks from the peak of infection (6 weeks after infection). This induces a latent infection phase with. . .

DRWD . . . In FIG. 2A, the immunization was given as a prophylactic vaccine 6 weeks before the mice were given a M. **tuberculosis** infection (approx. 250 bacilli) through the aerosol route with. Bacterial numbers in the lung was enumerated 6 weeks post infection.. .

DETD [0024] The invention is related to preventing, treating and detecting infections caused by species of the **tuberculosis** complex (Mycobacterium **tuberculosis**, M. bovis, M. africanum) by the use of a polypeptide comprising a M. **tuberculosis** antigen or an immunogenic portion or other variant thereof, or by the use of a DNA sequence encoding a M. **tuberculosis** antigen or an immunogenic portion or other variant thereof. The invention discloses a new therapeutic vaccine against **tuberculosis** comprising antigens induced during the latent stage of TB-infection. It also discloses a multiphase vaccine incorporating a combination of prophylactic and therapeutic antigens as well as diagnostic reagents for the detection of the latent stage of M. **tuberculosis** infection.

DETD . . . mycobacteria infection, which stage is characterized by low-oxygen tension in the microenvironment of the mycobacteria, for a therapeutic vaccine against **tuberculosis**.

DETD . . . with efficacy as prophylactic vaccines, where the fusion partner is selected from e.g. the group consisting of ESAT-6, TB10.4, CFP10, **RD1-ORF5**, RD1-ORF2, Rv1036, MPB64, MPT64, Ag85A, Ag85B (MPT59), MPB59, Ag85C, 19 kDa lipoprotein, MPT32.

DETD [0033] The invention further discloses a therapeutic vaccine against **tuberculosis** comprising one or more polypeptides or fragments

hereof, which polypeptides are expressed during the latent stage of the mycobacteria infection,. . .

DETD [0036] The invention also discloses a method for treating an animal, including a human being, with **tuberculosis** caused by virulent mycobacteria, e.g., by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, comprising administering to the animal the above-mentioned vaccine.

DETD [0037] The invention also discloses a method for immunizing an animal, including a human being, against **tuberculosis** caused by virulent mycobacteria, e.g., by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, comprising administering to the animal the above mentioned vaccine.

DETD . . . to whom the vaccine has been administered, the amount of expressed antigen being effective to confer substantially increased resistance to **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, in an animal, including a human being.

DETD . . . . use of a nucleic acid fragment according to the invention for the preparation of a composition for the diagnosis of **tuberculosis** caused by virulent mycobacteria, e.g., by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, and the use of a nucleic acid fragment according to the invention for the preparation of a pharmaceutical composition for the vaccination against **tuberculosis** caused by virulent mycobacteria, e.g., by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis.

DETD . . . a still further embodiment, the invention discloses a vaccine for immunizing an human being or other mammal or animal, against **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, comprising as the effective component a non-pathogenic microorganism, wherein at least one copy of a. . .

DETD [0049] (b) isolating the polypeptide from a whole mycobacterium, e.g. Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, from culture filtrate or from lysates or fractions thereof; or

DETD [0051] The invention also discloses a method of diagnosing **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, in an animal, including a human being, comprising intradermally injecting, in the animal, a polypeptide. . . immunogenic composition as defined above, a positive skin response at the location of injection being indicative of the animal having **tuberculosis**, and a negative skin response at the location of injection being indicative of the animal not having **tuberculosis** .

DETD [0052] In another embodiment, the invention discloses a method for immunizing an animal, including a human being, against **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, comprising administering to the animal the polypeptide as defined above, the immunogenic composition according to. . .

DETD . . . detecting binding of a antibody to said polypeptide, said binding being an indication that said subject is infected by Mycobacterium **tuberculosis** or is susceptible to Mycobacterium **tuberculosis** infection.

DETD [0082] A preferred polypeptide within the present invention is an immunogenic antigen from M. **tuberculosis** produced when the organism is subjected to the stresses associated with latent infection. Such antigen can for example also be derived from the M. **tuberculosis** cell and/or M. **tuberculosis** culture filtrate. Thus, a polypeptide comprising an immunogenic portion of one of the above antigens may consist entirely of the immunogenic portion, or may contain additional sequences. The additional sequences may be derived from the native M. **tuberculosis** antigen or be heterologous and such sequences may, but need not, be immunogenic.

DETD . . . any other antigen with which it is natively associated, i.e.

free of any other antigen from bacteria belonging to the **tuberculosis** complex or a virulent mycobacterium. This can be accomplished by preparing the polypeptide fragment by means of recombinant methods in. . .

DETD [0085] By the term "virulent mycobacterium" is understood a bacterium capable of causing the **tuberculosis** disease in an animal or in a human being. Examples of virulent mycobacteria include but are not limited to M. **tuberculosis**, M. africanum, and M. bovis. Examples of relevant animals are cattle, possums, badgers and kangaroos.

DETD [0088] By "a latently infected individual" is understood an individual, who has been infected by a virulent mycobacterium, e.g. M. **tuberculosis**, but shows no sign of active **tuberculosis** . It is likely that individuals who have been vaccinated, e.g. by BCG, or treated for TB may still retain the. . . for PPD reactivity. Nonetheless, in its most accurate sense, "latently-infected" may be used to describe any individual who has M. **tuberculosis** residing in their tissues but who is not clinically ill.

DETD [0101] In the context of providing candidate molecules for a new vaccine against **tuberculosis**, the subdominant epitopes are however as relevant as are the dominant epitopes since it has been shown (Olsen, 2000) that. . .

DETD . . . response may also be determined by the use of T cell lines derived from an immune individual or an M. **tuberculosis** -infected person where the T cell lines have been driven with either live mycobacteria, extracts from the bacterial cell or culture. . .

DETD [0114] In general, M. **tuberculosis** antigens, and DNA sequences encoding such antigens, may be prepared using any one of a variety of procedures.

DETD [0115] They may be purified as native proteins from the M. **tuberculosis** cell or culture filtrate by procedures such as those described above. Immunogenic antigens may also be produced recombinantly using a. . .

DETD . . . at least one fusion partner. The fusion partner can, in order to enhance immunogenicity, be another polypeptide derived from M. **tuberculosis**, such as of a polypeptide fragment derived from a bacterium belonging to the **tuberculosis** complex, such as ESAT-6, TB10.4, CFP10, **RD1-ORF5**, RD1-ORF2, Rv1036, MPB64, MPT64, Ag85A, Ag85B (MPT59), MPB59, Ag85C, 19 kDa lipoprotein, MPT32 and alpha-crystalline, or at least one T-cell. . .

DETD . . . to the invention, and solubilizing or dispersing the polypeptide in a medium for a vaccine, and optionally adding other M. **tuberculosis** antigens and/or a carrier, vehicle and/or adjuvant substance.

DETD . . . from M. leprae. Antigens with therapeutic properties may be identified based on their ability to diminish the severity of M. **tuberculosis** infection in experimental animals or prevent reactivation of previous infection, when administered as a vaccine. The composition used for therapeutic. . .

DETD [0161] Cloning and Expression of Low Oxygen Induced M. **tuberculosis** Antigens in E. coli.

DETD [0162] A number of M **tuberculosis** genes are induced under low oxygen conditions. The upregulation of the genes listed in table 2 has been determined at. . .

DETD . . . Ammonium Sulfate, 0.2 mM of each of the four nucleotides, 0.2 μM of each primer and 10 ng of M. **tuberculosis** H37Rv chromosomal DNA. The reaction mixtures were initially heated to 95° C. for 5 min., followed by 35 cycles of:. . .

DETD . . . with recombinant antigens. Six weeks after the last immunization, the mice are given an aerosol infection with approximately 250 M. **tuberculosis** bacilli. The protective capacity of the vaccine is evaluated by enumeration of the bacteria in spleen and lung 6 weeks. . .

DETD . . . reactivation model of latent TB has been established (van Pinxteren, 2000) (FIG. 1B). An aerosol infection with approximately 250 M. **tuberculosis** bacilli is given and at the peak of infection 6 weeks later, the mice receive an 8-week course of anti-mycobacterial. . .

DETD . . . cells is significantly higher in the unimmunized group. ESAT6

is an antigen produced in high amounts by the actively-growing M. **tuberculosis** bacteria. The level of the ESAT6 specific immune response in infected mice could therefore be indicative the degree of actively-growing. . . have in fact demonstrated such a correlation between the level of ESAT6 response and degree of disease in both M. **tuberculosis**-infected humans and M. bovis-infected cattle (Doherty, 2002, Vordermeier, 2002). Therefore, the higher ESAT6 response in the unimmunized group of latently-infected. . .

DETD . . . lungs of the Rv0569 vaccinated mice, whereas neither ESAT6 nor BCG are able to inhibit the growth of the M. **tuberculosis** bacteria when given as a vaccine during latent infection. That is, the induction of Rv0569 T cell responses can participate. . .

DETD [0182] Anon. 2001. Global **Tuberculosis** Control. WHO Report.

DETD [0202] Danish Patent application PA 2000 00666 "Nucleic acid fragments and polypeptide fragments derived from M. **tuberculosis**"

DETD [0203] Danish Patent application PA 1999 01020 (WO 01/23388) " **Tuberculosis** vaccine and diagnostic based on the Mycobacterium **tuberculosis** esat-6 gene family".

DETD [0204] Patent application U.S. Ser. No. 09/0505,739 "Nucleic acid fragments and polypeptide fragments derived from M. **tuberculosis** "

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 1
LENGTH: 273
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 1
Val Glu Pro Lys Arg Ser Arg Leu Val Val Cys Ala Pro Glu Pro Ser
1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 2
LENGTH: 152
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 2
Met Ser Pro Gly Ser Arg Arg Ala Ser Pro Gln Ser Ala Arg Glu Val
1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 3
LENGTH: 114
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 3
Val Glu Ser Glu Pro Leu Tyr Lys Leu Lys Ala Glu Phe Phe Lys Thr
1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 4
LENGTH: 344
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 4
Met Pro Ile Ala Thr Pro Glu Val Tyr Ala Glu Met Leu Gly Gln Ala
1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 5
LENGTH: 113
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 5
Met Gly Glu His Ala Ile Lys Arg His Met Arg Gln Arg Lys Pro Thr
1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 6
LENGTH: 380
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 6
Val Ala Gly Asn Pro Asp Val Val Thr Val Leu Leu Gly Gly Asp Val

1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 7
LENGTH: 397
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 7
Val Thr Asp His Val Arg Glu Ala Asp Asp Ala Asn Ile Asp Asp Leu
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 8
LENGTH: 446
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 8
Met Val Glu Pro Gly Asn Leu Ala Gly Ala Thr Gly Ala Glu Trp Ile
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 9
LENGTH: 210
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 9
Met Ile Ala Thr Thr Arg Asp Arg Glu Gly Ala Thr Met Ile Thr Phe
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 10
LENGTH: 80
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 10
Met Thr Asn Val Gly Asp Gln Gly Val Asp Ala Val Phe Gly Val Ile
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 11
LENGTH: 652
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 11
Val Thr Val Thr Pro Arg Thr Gly Ser Arg Ile Glu Glu Leu Leu Ala
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 12
LENGTH: 395
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 12
Met Arg Gly Gln Ala Ala Asn Leu Val Leu Ala Thr Trp Ile Ser Val
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 13
LENGTH: 94
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 13
Met Cys Gly Asp Gln Ser Asp His Val Leu Gln His Trp Thr Val Asp
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 14
LENGTH: 560
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 14
Met Ile Pro Thr Met Thr Ser Ala Gly Trp Ala Pro Gly Val Val Gln
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 15
LENGTH: 143

TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 15
Met Ile Thr Asn Leu Arg Arg Arg Thr Ala Met Ala Ala Ala Gly Leu
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 16
LENGTH: 905
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 16
Leu Ser Ala Ser Val Ser Ala Thr Thr Ala His His Gly Leu Pro Ala
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 17
LENGTH: 258
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 17
Met Ser Phe His Asp Leu His His Gln Gly Val Pro Phe Val Leu Pro
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 18
LENGTH: 285
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 18
Val Val Lys Arg Ser Arg Ala Thr Arg Leu Ser Pro Ser Ile Trp Ser
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 19
LENGTH: 285
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 19
Val Val Lys Arg Ser Arg Ala Thr Arg Leu Ser Pro Ser Ile Trp Ser
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 20
LENGTH: 114
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 20
Val Thr Tyr Val Ile Gly Ser Glu Cys Val Asp Val Met Asp Lys Ser
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 21
LENGTH: 279
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 21
Met Asn Gln Ser His Lys Pro Pro Ser Ile Val Val Gly Ile Asp Gly
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 22
LENGTH: 339
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 22
Met Thr Glu Pro Ala Ala Trp Asp Glu Gly Lys Pro Arg Ile Ile Thr
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 23
LENGTH: 681
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 23
Val Leu Met Thr Ala Ala Ala Asp Val Thr Arg Arg Ser Pro Arg Arg

1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 24
LENGTH: 144
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 24
Met Ala Thr Thr Leu Pro Val Gln Arg His Pro Arg Ser Leu Phe Pro
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 25
LENGTH: 331
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 25
Met Pro Asp Thr Met Val Thr Thr Asp Val Ile Lys Ser Ala Val Gln
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 26
LENGTH: 195
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 26
Met Pro Leu Leu Thr Ile Gly Asp Gln Phe Pro Ala Tyr Gln Leu Thr
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 27
LENGTH: 272
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 27
Met Ser Gly Arg Gly Glu Pro Thr Met Lys Thr Ile Ile Val Gly Ile
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 28
LENGTH: 393
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 28
Met Arg Asp Ala Ile Pro Leu Gly Arg Ile Ala Gly Phe Val Val Asn
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 29
LENGTH: 413
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 29
Met Ala Ser Ser Ala Ser Asp Gly Thr His Glu Arg Ser Ala Phe Arg
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 30
LENGTH: 120
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 30
Met Ser Thr Gln Arg Pro Arg His Ser Gly Ile Arg Ala Val Gly Pro
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 31
LENGTH: 374
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 31
Met Arg Ser Glu Arg Leu Arg Trp Leu Val Ala Ala Glu Gly Pro Phe
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 32
LENGTH: 179

TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 32
Met Leu His Arg Asp Asp His Ile Asn Pro Pro Arg Pro Arg Gly Leu
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 33
LENGTH: 375
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 33
Val Thr Gln Thr Gly Lys Arg Gln Arg Arg Lys Phe Gly Arg Ile Arg
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 34
LENGTH: 371
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 34
Met Arg Val Gly Ile Pro Thr Glu Thr Lys Asn Asn Glu Phe Arg Val
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 35
LENGTH: 104
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 35
Met Val Ile Arg Phe Asp Gln Ile Gly Ser Leu Val Leu Ser Met Lys
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 36
LENGTH: 344
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 36
Val Leu Lys Asn Ala Val Leu Leu Ala Cys Arg Ala Pro Ser Val His
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 37
LENGTH: 336
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 37
Val Trp Ser Ala Ser Gly Gly Gln Cys Gly Lys Tyr Leu Ala Ala Ser
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 38
LENGTH: 110
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 38
Val Val Gln Gly Arg Thr Val Leu Phe Arg Thr Ala Glu Gly Ala Lys
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 39
LENGTH: 463
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 39
Met Asn His Leu Thr Thr Leu Asp Ala Gly Phe Leu Lys Ala Glu Asp
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 40
LENGTH: 332
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 40
Met Asn Thr His Phe Pro Asp Ala Glu Thr Val Arg Thr Val Leu Thr

1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 41
LENGTH: 578
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 41
Met Thr Thr Gly Gly Leu Val Asp Glu Asn Asp Gly Ala Ala Met Arg
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 42
LENGTH: 268
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 42
Met Ser Asp Pro Arg Pro Ala Arg Ala Val Val Val Gly Ile Asp Gly
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 43
LENGTH: 181
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 43
Met Thr Glu Tyr Glu Gly Pro Lys Thr Lys Phe His Ala Leu Met Gln
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 44
LENGTH: 274
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 44
Met Thr Trp Ala Asp Glu Val Leu Ala Gly His Pro Phe Val Val Ala
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 45
LENGTH: 248
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 45
Val Ser Asp Gly Glu Gln Ala Lys Ser Arg Arg Arg Arg Gly Arg Arg
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 46
LENGTH: 819
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 46
gtggaaccga aacgcagtcg cctcgtcgta tgtgcacccg agccatcgca cgcgcgggaa 60
ttcccggatg tcgccgtatt ctccggcggc cgggctaacg catcccaggc cgaacggttg 120
gctcgtgccg tgggtcgcgt gttggccgat cggggcgtca ccgggggtgc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 47
LENGTH: 819
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 47
gtggaaccga aacgcagtcg cctcgtcgta tgtgcacccg agccatcgca cgcgcgggaa 60
ttcccggatg tcgccgtatt ctccggcggc cgggctaacg catcccaggc cgaacggttg 120
gctcgtgccg tgggtcgcgt gttggccgat cggggcgtca ccgggggtgc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 48
LENGTH: 342
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 48
gtggagtccg aaccgctgta caagctcaag gcggagttct tcaaaaccct tgcgcatccg 60
gcgcggatca ggattttgga gctgctggtc gagcgggacc gttcggtcgg tgagttgctg 120
tcctcggacg tcggcctgga gtcgtcgaac ctgtcccagc agctgggtgt. . .

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 49
LENGTH: 1032
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 49
atgcctatcg caacgcccga ggtctacgcg gagatgctcg gtcaggccaa acaaaactcg 60
tacgctttcc cggctatcaa ctgcacctcc tcggaaaccg tcaacgccgc gatcaaaggt 120
ttcgccgacg ccggcagtga cggaatcatc cagttctcga ccggtggcgc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 50
LENGTH: 339
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 50
atgggtgagc acgccatcaa gcggcacatg cggcaacgga agcctacgaa gcatccccta 60
gcccagaaac ggggcgcgcg gattctggtc ttcaccgacg atccccgcag gagcgtcctc 120
atagtgcccg gttgccacct ggattccatg cgccgagaaa agaacgcgta. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 51
LENGTH: 1140
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 51
gtggctggca atcctgatgt ggtgacggtg ctgctgggcg gtgacgtcat gctcggccgt 60
ggcgtcgatc agatcctgcc tcatcccggc aaaccgcaat tgcgcgaacg gtatatgcgg 120
gatgcgaccg gctatgttcg cctggccgag cgggtgaacg ggcgcattcc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 52
LENGTH: 1191
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 52
gtgacagacc acgtgcgcga ggcggacgac gcgaacatcg acgatctgtt gggcgacctg 60
ggcggtaccg cgcgcgccga gcgtgcgaag cttgtcgagt ggttgctcga gcagggcatc 120
acccccgacg agattcgggc gaccaacccg ccgttgctgc tggccacccg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 53
LENGTH: 1338
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 53
atggtagagc ccggcaattt ggcaggcgcg accggcgccg aatggatcgg ccggccaccg 60
cacgaggaat tgcagcgcaa agtgcgcccg ctgctgccat ccgacgatcc gttctacttc 120
ccacctgccg gctaccagca tgccgtgccc ggaacggtgt tgcgctcgcg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 54
LENGTH: 630
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 54
atgatcgcca caacccgcga tcgtgaagga gccaccatga tcacgtttag gctgcgcttg 60
ccgtgccgga cgatactgcg ggtgttcagc cgcaatccgc tggtgcgtgg gacggatcga 120
ctcgaggcgg tcgtcatgct gctggccgtc acggtctcgc tgctgactat. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 55
LENGTH: 240
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 55
atgaccaacg tcggtgacca gggggttgac gcggtcttcg gggtgatcta cccacctcag 60
gtcgcgctgg tcagtttcgg caagccggca caacgagttt gcgccgtcga cggcgcgatc 120
cacgtcatga cgaccgtgct ggctacgctg cccgctgacc acggctgcag. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 56
LENGTH: 1956
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 56
gtgacggtga caccacggac cggcagccgc atcgaggagc tgcttgcacg cagcggccgg 60
ttcttcatcc cgggtgagat ctcggcggat ctgcgtaccg tgacccgccg cggcggccgc 120
gacggcgacg tgttctatcg agaccggtgg agccacgaca aggtggtccg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 57
LENGTH: 1185
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 57
atgagagggc aagcggccaa tctcgtgctg gccacctgga tctcggtggt caacttctgg 60
gcgtggaacc tgatcggccc gctgtcgacc agctacgcgc gtgacatgtc actgtccagc 120
gccgaggcgt cgctgctcgt cgccaccccg atcctggtgg gtgcccttgg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 58
LENGTH: 282
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 58
atgtgcggcg accagtcgga tcacgtgctg cagcactgga ccgtcgacat atcgatcgac 60
gaacacgaag gattgactcg ggcgaaggca cggctgcgtt ggcgggaaaa ggaattggtg 120
ggtgttggcc tggcaaggct caatccggcc gaccgcaacg tccccgagat. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 59
LENGTH: 1680
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 59
atgattccca cgatgacatc ggccggctgg gcaccagggg tggtgcagtt ccgcgaatac 60
caacggcgtt ggctgcgcgg cgatgtcctc gccggcctga ccgtggccgc ctatctgatc 120
ccgcaagcga tggcgtatgc gaccgtggcg ggcctaccgc cggcagccgg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 60
LENGTH: 429
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 60
atgatcacaa acctccgacg ccgaaccgcg atggcagccg ccggcctagg ggctgctctc 60
gggctgggca tcctgctggt tccgacggtg gacgcccatc tcgccaacgg ttcgatgtcg 120
gaagtcatga tgtcggaaat tgccgggttg cctatccctc cgattatcca. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 61
LENGTH: 2715
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 61
ttgtcggcgt cagtgtctgc cacgacggct catcatggct tgccagcaca tgaagtggtg 60
ctgctgctgg agagcgatcc atatcacggg ctgtccgacg gcgaggccgc ccaacgacta 120
gaacgcttcg ggcccaacac cttggcggtg gtaacgcgcg ctagcttgct. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 62
LENGTH: 774
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 62
atgagtttcc acgatcttca tcaccaaggt gttccgttcg tgttgcccaa cgcctgggat 60
gtgccgtcgg ccctggccta cctcgcggag ggcttcacgg ctatcggcac aaccagtttc 120
ggggtctcgt ccagcggcgg gcacccggac gggcaccgcg ccactcgcgg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 63
LENGTH: 855
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 63
gtggtcaagc gctctcgggc aacccgactt tcgccgagca tctggtccgg atgggaatca 60
cctcagtgtc ggtccattcg ggcgcgattg ctgctacccc ggggtcggtc gcggccgccg 120
aacgccgatt gttgctggaa tcagctcgcg gtgacgcctg acacccggat. . .
DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 64
LENGTH: 885
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 64
atgtctaaac cccgcaagca gcacggagtt gtcgtcgggg tagatggttc gctcgaatcg 60
gatgccgccg cctgttgggg tgccaccgat gcggcgatga ggaacattcc gctgaccgtg 120
gtccacgtgg tgaacgccga tgtagcgacg tggccgccga tgccgtatcc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 65
LENGTH: 342
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 65
gtgacctatg tgatcggtag tgagtgcgtg gatgtgatgg acaagtcctg tgtgcaggag 60
tgtccggtcg actgtatcta tgagggcgcc cgaatgctct acatcaaccc cgacgagtgc 120
gtggattgtg gtgcgtgcaa accggcctgc cgcgtcgagg cgatctactg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 66
LENGTH: 837
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 66
atgaaccaat cacacaaacc cccatcgatc gtcgtcggta ttgatggctc gaagccggcc 60
gtgcaagccg cactgtgggc ggtcgacgag gcagccagcc gtgacatccc gctgcgtctg 120
ctgtacgcga tcgaacccga cgatcccggg tacgccgcac acggcgcggc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 67
LENGTH: 1017
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 67
atgacggagc cagcggcgtg ggacgaaggc aagccgcgaa tcatcacttt gaccatgaac 60
cccgccttgg acatcacgac gagcgtcgac gtggtgcgcc cgaccgagaa aatgcgttgt 120
ggcgcacctc gctacgatcc cggcggcggc ggtatcaatg tcgcccgcat. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 68
LENGTH: 2043
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 68
gtgctgatga ccgcagcggc tgatgtcacc cggcgctcgc cgcggcgcgt gttccgtgac 60
cgccgcgagg ccggccgggt gctggcggaa ttactcgccg cctatcggga ccagccggac 120
gtgattgtgc tcggcttggc ccggggtggc ctcccggtcg catgggaggt. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 69
LENGTH: 432
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 69
atggccacca cccttcccgt tcagcgccac ccgcggtccc tcttccccga gttttctgag 60
ctgttcgcgg ccttcccgtc attcgccgga ctccggccca ccttcgacac ccggttgatg 120
cggctggaag acgagatgaa agaggggcgc tacgaggtac gcgcggagct. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 70
LENGTH: 993
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 70
atgccggaca ccatggtgac caccgatgtc atcaagagcg cggtgcagtt ggcctgccgc 60
gcaccgtcgc tccacaacag ccagccctgg cgctggatag ccgaggacca cacggttgcg 120
ctgttcctcg acaaggatcg ggtgctttac gcgaccgacc actccggccg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 71
LENGTH: 585
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 71

atgccactgc taaccattgg cgatcaattc cccgcctacc agctcaccgc tctcatcggc 60
ggtgacctgt ccaaggtcga cgccaagcag cccggcgact acttcaccac tatcaccagt 120
gacgaacacc caggcaagtg gcgggtggtg ttcttttggc cgaaagactt. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 72
LENGTH: 816
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 72
atgtctggga gaggagagcc gacgatgaaa acaatcattg ttggtatcga tggttcgcac 60
gcggcgatta cggccgcatt gtgggggttt gacgaggcca tcagccgagc ggtgccgctg 120
cgactggtct cagtgatcaa gccgacacat ccgtccccgg acgactacga. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 73
LENGTH: 1179
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 73
atgcgtgatg cgatcccgct tgggcggatc gccgggtttg tggtgaacgt ccactggagc 60
gtgttggtga tcctgtggtt gttcacctgg agtctggcga ccatgttgcc gggtaccgtc 120
ggaggctacc cggccgtggt ctattggctt ctcggcgcag gtggcgcggt. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 74
LENGTH: 1239
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 74
atggcaagtt ctgcgagcga cggcacccac gaacgctcgg cttttcgcct gagtccaccg 60
gtcttgagcg gcgccatggg accgttcatg cacaccggtc tgtacgtcgc tcaatcgtgg 120
cgcgactatc tgggtcaaca gcccgataaa ctgccgatcg cacggcccac. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 75
LENGTH: 360
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 75
atgtccacgc aacgaccgag gcactccggt attcgggctg ttggccccta cgcatgggcc 60
ggccgatgtg gtcggatagg caggtggggg gtgcaccagg aggcgatgat gaatctagcg 120
atatggcacc cgcgcaaggt gcaatccgcc accatctatc aggtgaccga. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 76
LENGTH: 1122
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 76
atgcgatcag aacgtctccg gtggctggta gccgcagaag gtccgttcgc ctcggtgtat 60
ttcgacgact cgcacgacac tcttgatgcc gtcgagcgcc gggaagcgac gtggcgcgat 120
gtccggaagc atctcgaaag ccgcgacgcg aagcaggagc tcatcgacag. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 77
LENGTH: 537
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 77
atgctgcacc gcgacgatca catcaatccg ccgcggcccc gcgggttgga tgttccttgc 60
gcccgcctac gagcgacaaa tcccctgcgc gccttggcgc gttgcgttca ggcgggcaag 120
ccgggcacca gttcagggca tcggtccgtg ccgcatacgg cggacttgcg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 78
LENGTH: 1125
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 78
gtgacgcaaa ccggcaagcg tcagagacgc aaattcggtc gcatccgaca gttcaactcc 60
ggccgctggc aagccagcta caccggcccc gacggccgcg tgtacatcgc ccccaaaacc 120
ttcaacgcca agatcgacgc cgaagcatgg ctcaccgacc gccgccgcga. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 79

LENGTH: 1113
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 79
atgcgcgtcg gtattccgac cgagaccaaa aacaacgaat tccgggtggc catcaccccg 60
gccggcgtcg cggaactaac ccgtcgtggc catgaggtgc tcatccaggc aggtgccgga 120
gagggctcgg ctatcaccga cgcggatttc aaggcggcag gcgcgcaact. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 80
LENGTH: 312
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 80
atggtcatcc ggtttgatca aatagggtca ttggtcctct caatgaaatc ccttgcgtca 60
ctgtcgtttc agcggtgtct gcgcgagaat tctagtttgg tcgcggcgct ggaccggctc 120
gatgctgcgg tcgatgagct gagcgctttg tcgtttgatg cgttgaccac. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 81
LENGTH: 1032
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 81
gtgctcaaga acgcagtctt gctggcatgc cgggcgccgt cggtgcacaa cagccagccc 60
tggcgttggg tggccgaaag cggctccgag cacactactg tgcacctgtt cgtcaaccgc 120
caccgaacgg tgccggccac cgaccattcc ggccggcaag cgatcatcag. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 82
LENGTH: 1011
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 82
gtgtggtccg cctcgggtgg gcagtgcggg aagtatcttg ccgcctcgat ggtgctgcag 60
cttgatgggt tggaacgtca cggtgtgttg gagtttgggc gtgaccgcta tggccccgag 120
gtgcgtgagg agctgttggc gatgagtgcg gccagcatcg atcgttatct. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 83
LENGTH: 330
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 83
gtggtgcaag gccgcaccgt gctgtttcgt accgcggagg gcgccaaatt attttcagcc 60
gtcgcgaagt gcgcggtggc tttcgaggcg gacgaccaca acgttgccga gggctggagc 120
gtgatcgtca aggttcgcgc ccaggtgctg acgaccgacg cgggggtccg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 84
LENGTH: 1389
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 84
atgaatcacc taacgacact tgacgccggg tttctcaagg cagaagacgt ggatcggcac 60
gtgagtctgg caatcggcgc tctggcggtc atcgaggggc cggctcccga tcaggaagcc 120
ttcttatcgt cgctcgctca acgcctacgt ccctgtaccc ggttcgggca. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 85
LENGTH: 996
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 85
atgaacaccc atttcccgga cgccgaaacc gtgcgaacgg ttctcaccct ggccgtccgg 60
gccccctcca tccacaacac gcagccgtgg cggtggcggg tatgcccgac gagtctggag 120
ctgttctcta gacccgatat gcagctgcgt agcaccgatc cggacgggcg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 86
LENGTH: 1734
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 86
atgacaacag ggggcctcgt cgacgaaaac gacggcgccg caatgcgtcc actgcgtcac 60

acgctctccc aactacgcct gcacgagctg ctggtcgagg tgcaggaccg ggtcgagcag 120
atcgtcgagg gccgggaccg cctcgatggt ctggtggagg ccatgctcgt. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 87
LENGTH: 804
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 87
atgagcgatc ctcggccagc tcgggcagtg gtcgttggta tcgacgggtc aagggcggca 60
acgcatgcgg cgttgtgggc ggtcgatgag gcggtgaacc gagacattcc gctgcgactg 120
gtgtacgtca tcgatccgtc ccaactgtcc gccgccggcg agggcggtgg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 88
LENGTH: 543
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 88
atgacagaat acgaagggcc taagacaaaa ttccacgcgt taatgcagga acagattcat 60
aacgaattca cagcggcaca acaatatgtc gcgatcgcgg tttatttcga cagcgaagac 120
ctgccgcagt tggcgaagca tttttacagc caagcggtcg aggaacgaaa. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 89
LENGTH: 822
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 89
atgacatggg ccgacgaggt gctcgccgga catccctttg tggttgctca ccgtggtgcg 60
tcggcggctc ggccggagca tacccttgcc gcctacgacc tggcgctcaa agagggcgcc 120
gacggcgtgg aatgtgatgt gcggttgacc cgggacgggc atctggtctg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 90
LENGTH: 744
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 90
gtgtccgacg gcgaacaagc caaatcacgt cgacgccggg ggcggcgccg cgggcggcgc 60
gctgcggcta cagccgagaa tcacatggac gcccaaccgg ccggcgacgc caccccgacc 120
ccggcaacgg cgaagcggtc ccggtcccgc tcacctcgtc gcgggtcgac. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 91
LENGTH: 88
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 91
Met Lys Ala Lys Val Gly Asp Trp Leu Val Ile Lys Gly Ala Thr Ile
1 5 10. . .
CLM What is claimed is:
1. A method for inducing an immune response to latent **tuberculosis** in an individual, said method comprising the step of delivering a composition comprising one or more polypeptides or fragments thereof,. . .
2. The method according to claim 1, wherein said individual is infected by a virulent mycobacterium, e.g. M. **tuberculosis**, and is not vaccinated with BCG against **tuberculosis**.

6. A therapeutic vaccine against **tuberculosis** comprising one or more polypeptides or fragments hereof, which polypeptides are expressed during the latent stage of the mycobacteria infection,. . .
. . . vaccine according to claim 9 where the fusion partners is selected from the group consisting of ESAT-6, ESAT-6-Ag85B, TB10.4, CFP10, **RD1-ORF5**, RD1-ORF2, Rv1036, MPB64, MPT64, Ag85A, Ag85B (MPT59), MPB59, Ag85C, 19 kDa lipoprotein, MPT32.

. . . 13. A multiphase vaccine according to claim 12 where the antigen components with prophylactic activity comprises ESAT-6, ESAT-6-Ag85B, TB10.4, CFP10, **RD1-ORF5**, RD1-ORF2, Rv1036, MPB64, MPT64, Ag85A, Ag85B (MPT59), MPB59, Ag85C, 19 kDa lipoprotein or MPT32.

18. A method for treating an animal, including a human being, with **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, comprising administering to the animal the vaccine according to claim 6.

19. A method for immunizing an animal, including a human being, against **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, comprising administering to the animal the vaccine according to claim 12.

20. A method of diagnosing **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, in an animal, including a human being, comprising application or intradermally injecting, in the animal,. . . encoding these polypeptides, a positive skin response at the location of injection or application being indicative of the animal having **tuberculosis**, and a negative skin response at the location of injection or application being indicative of the animal not having **tuberculosis**.

22. A method of diagnosing Mycobacterium **tuberculosis** infection in a subject comprising: (a) contacting a polypeptides or fragments hereof, which polypeptides are expressed during the latent stage. . . detecting binding of an antibody to said polypeptide, said binding being an indication that said subject is infected by Mycobacterium **tuberculosis** or is susceptible to Mycobacterium **tuberculosis** infection.

L13 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3
AN 2003:696302 CAPLUS
DN 139:229237
TI Protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment
IN Andersen, Peter; Weldingh, Karin; Hansen, Christina Veggerby; Florio, Walter; Okkels, Li Mei Meng; Skjot, Rikke Louise Vinther; Rasmussen, Peter Birk
PA Den.
SO U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Ser. No. 60,428. CODEN: USXXCO
DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003165525	A1	20030904	US 2002-138473	20020502
	US 6641814	B1	20031104	US 1998-50739	19980330
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	US 2002094336	A1	20020718	US 2001-791171	20010220
PRAI	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-50739	A2	19980330		
	DK 1998-1281	A	19981008		
	US 2001-791171	B2	20010220		
	US 2002-60428	A2	20020129		
	EP 1998-913536	A3	19980401		

AB The present invention is based on the identification and characterization of 9 antigens, including Rv0652/CFP16, Rv2462c/TB51, Rv1984c/CFP21, Rv2185c/TB16, Rv1636/TB15A, Rv3451/CFP23, Rv3872/RD1-ORF3, Rv3354/CFP8A and Rv2623/TB32, from Mycobacterium **tuberculosis**. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing

the polypeptides. The invention related to diagnosing **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, in an animal, including a human being. The invention related to treating **tuberculosis** using antigens isolated from Mycobacterium **tuberculosis**.

TI Protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment

AB The present invention is based on the identification and characterization of 9 antigens, including Rv0652/CFP16, Rv2462c/TB51, Rv1984c/CFP21, Rv2185c/TB16, Rv1636/TB15A, Rv3451/CFP23, Rv3872/RD1-ORF3, Rv3354/CFP8A and Rv2623/TB32, from Mycobacterium **tuberculosis**. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, in an animal, including a human being. The invention related to treating **tuberculosis** using antigens isolated from Mycobacterium **tuberculosis**.

ST Mycobacterium antigen sequence **tuberculosis** diagnosis treatment

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(Ag85A, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(Ag85B, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(Ag85C, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(CFP10, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ESAT-6, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(MPB59, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(MPB64, in fusion protein; protein and DNA sequences of antigens from

Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(MPT32, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(MPT64, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(RD1-ORF2, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**RD1-ORF5**, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Rv0652/CFP16; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(Rv1036, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Rv1636/TB15A; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Rv1984c/CFP21; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Rv2185c/TB16; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study,

unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Rv2462c/TB51; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Rv2623/TB32; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Rv3354/CFP8A; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Rv3451/CFP23; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Rv3872/RD1-ORF3; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(TB10.4, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Diagnosis
(agents, **tuberculosis**; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Cell membrane
Cell wall
(antigen isolated from; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Fusion proteins (chimeric proteins)
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(antigens in; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Cytoplasm
(cytosol, antigen isolated from; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Animal
Human
(diagnosis of **tuberculosis** in; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Mycobacterium avium
Mycobacterium intracellulare
Mycobacterium marinum

Mycobacterium scrofulaceum
Mycobacterium szulgai
Mycobacterium xenopi
(expression of antigen CFP21 and CFP23 in; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Mycobacterium fortuitum
Mycobacterium kansasii
(expression of antigen CFP23 in; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Diagnosis
(immunodiagnosis; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Lipoproteins
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antibodies and Immunoglobulins
RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(monoclonal; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT DNA sequences
Epitopes
Immunoassay
Molecular cloning
Mycobacterium **tuberculosis**
Protein sequences
Tuberculosis
Tuberculostatics
(protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antibodies and Immunoglobulins
RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Gene, microbial
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Diagnosis
(serodiagnosis; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Mycobacterium africanum
Mycobacterium bovis
Mycobacterium **tuberculosis**
(**tuberculosis** caused by; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Mycobacterium
(virulent; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Crystallins
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(α-, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT 592558-08-2P 592558-09-3P 592558-10-6P 592558-11-7P 592558-12-8P

592558-13-9P 592558-14-0P 592558-15-1P 592558-16-2P, Antigen T51 (Mycobacterium **tuberculosis**)
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT 592557-99-8 592558-00-4 592558-01-5 592558-02-6 592558-03-7
592558-04-8 592558-05-9 592558-06-0 592558-07-1
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT 592573-15-4 592573-16-5 592573-17-6 592573-18-7 592573-19-8
592573-20-1 592573-21-2 592573-22-3 592573-23-4 592573-24-5
592573-26-7 592573-27-8 592573-28-9 592573-29-0 592573-30-3
592573-31-4 592573-32-5 592573-33-6
RL: PRP (Properties)
(unclaimed nucleotide sequence; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT 592573-14-3 592573-25-6
RL: PRP (Properties)
(unclaimed protein sequence; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT 213992-11-1 213992-15-5 264285-55-4 264285-57-6 264285-59-8
RL: PRP (Properties)
(unclaimed sequence; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

L13 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4
AN 2003:609858 CAPLUS
DN 139:163576
TI Mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of the **tuberculosis** complex
IN Andersen, Peter; Skjot, Rikke Louise Vinther
PA Den.
SO U.S. Pat. Appl. Publ., 135 pp., Cont.-in-part of U.S. Ser. No. 289,388, abandoned.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 10

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003147897	A1	20030807	US 2001-804980	20010313
WO 9501441	A1	19950112	WO 1994-DK273	19940701
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, CZ, DE, DE, DK, DK, ES, FI, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, SK, TJ, TT, UA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
EP 1508339	A1	20050223	EP 2004-77505	19940701
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI				
US 5955077	A	19990921	US 1995-465640	19950605
EP 1449922	A2	20040825	EP 2004-76605	19980401
EP 1449922	A3	20041117		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
US 2004013685	A1	20040122	US 2001-872505	20010601

PRAI DK 1993-798 A 19930702
US 1993-123182 B2 19930920
WO 1994-DK273 A2 19940701
US 1995-465640 A1 19950605
DK 1997-376 A 19970402
US 1997-44624P P 19970418
DK 1997-1277 A 19971110
US 1998-70488P P 19980105
US 1999-289388 B2 19990412
EP 1994-919574 A3 19940701
EP 1998-913536 A3 19980401
US 1998-246191 B2 19981230
DK 1999-1020 A 19990713
US 1999-144011P P 19990715
US 2000-615947 A2 20000713
WO 2000-DK398 A2 20000713
US 2001-804980 A2 20010313

AB The present invention is based on the identification and characterization of a number of novel M. **tuberculosis** derived proteins and protein fragments, e.g. TB10.3 (ORF7-1 or Rv3019c), TB10.4 (CFP7 or Rv0288) and TB12.9 (ORF7-2 or Rv3017c), ESAT-6, MPT64, CFP10, **RD1-ORF5**, RD1-ORF2, Rv1036, Ag85A, Ag85B, Ag85C, 19 kDa lipoprotein, MPT32, MPB59 and α-crystallin. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides.

TI Mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of the **tuberculosis** complex

AB The present invention is based on the identification and characterization of a number of novel M. **tuberculosis** derived proteins and protein fragments, e.g. TB10.3 (ORF7-1 or Rv3019c), TB10.4 (CFP7 or Rv0288) and TB12.9 (ORF7-2 or Rv3017c), ESAT-6, MPT64, CFP10, **RD1-ORF5**, RD1-ORF2, Rv1036, Ag85A, Ag85B, Ag85C, 19 kDa lipoprotein, MPT32, MPB59 and α-crystallin. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides.

ST Mycobacterium **tuberculosis** antigen gene antibody vaccine diagnosis skin test

; DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of the **tuberculosis** complex)

IT 575512-14-0 575512-20-8 575512-21-9 575512-22-0 575512-23-1
575512-24-2 575512-25-3 575512-26-4 575512-27-5 575512-28-6
575512-29-7 575512-30-0 575512-31-1 575512-32-2 575512-33-3
575512-34-4 575512-35-5 575512-36-6 575512-37-7 575512-38-8
575512-39-9 575512-40-2 575512-41-3 575512-43-5 575512-45-7
575512-47-9 575512-49-1 575512-51-5 575512-53-7 575512-55-9
575512-57-1 575512-59-3 575512-66-2 575512-67-3 575512-68-4
575512-69-5 575512-70-8 575512-71-9 575512-72-0 575512-73-1
575512-74-2 575512-75-3 575512-76-4 575512-77-5 575512-78-6
575512-79-7 575512-80-0 575512-81-1 575512-82-2 575512-83-3
575512-84-4 575512-85-5 575512-86-6 575512-87-7 575512-88-8
575512-89-9 575512-90-2 575512-91-3 575512-92-4 575512-93-5
575512-94-6 575512-95-7 575512-96-8 575512-97-9 575513-00-7
575513-01-8 575513-02-9 575513-03-0 575513-04-1 575513-05-2
575513-06-3 575513-07-4 575513-08-5 575513-10-9 575513-12-1
575513-14-3 575513-15-4 575513-16-5 575513-17-6 575513-18-7
575513-19-8 575513-20-1 575513-21-2 575513-22-3 575513-23-4
575513-24-5 575513-25-6 575513-26-7 575513-27-8 575513-32-5
575513-34-7 575513-36-9 575513-37-0 575513-39-2 575513-40-5
575513-41-6 575513-42-7 575513-43-8 575513-44-9 575513-45-0
RL: PRP (Properties)
(unclaimed nucleotide sequence; mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused

by species of the **tuberculosis** complex)

IT 575512-15-1 575512-16-2 575512-17-3 575512-18-4 575512-19-5
575512-42-4 575512-44-6 575512-46-8 575512-48-0 575512-50-4
575512-52-6 575512-54-8 575512-56-0 575512-58-2 575512-60-6
575512-61-7 575512-62-8 575512-63-9 575512-64-0 575512-65-1
575512-98-0 575512-99-1 575513-09-6 575513-11-0 575513-13-2
575513-29-0 575513-30-3 575513-31-4 575513-33-6 575513-35-8
575513-38-1
RL: PRP (Properties)
(unclaimed protein sequence; mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of the **tuberculosis** complex)

IT 213992-07-5 213992-08-6 213992-10-0 213992-11-1 213992-13-3
213992-14-4 213992-15-5 213992-16-6 213992-17-7 213992-18-8
213992-19-9 213992-20-2 213992-21-3 213992-23-5 213992-24-6
RL: PRP (Properties)
(unclaimed sequence; mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of the **t**

SYSTEM LIMITS EXCEEDED

L13 ANSWER 7 OF 10 USPATFULL on STN
AN 2003:291011 USPATFULL
TI Nucleic acids fragments and polypeptide fragments derived from M. ***tuberculosis
IN Andersen, Peter, Br.o slashed.nsh.o slashed.j, DENMARK
Niélsen, Rikke, Frederiksberg, DENMARK
Oettinger, Thomas, Hellerup, DENMARK
Rasmussen, Peter Birk, K.o slashed.benhaven, DENMARK
Rosenkrands, Ida, K.o slashed.benhaven, DENMARK
Weldingh, Karin, K.o slashed.benhaven, DENMARK
Florio, Walter, Frederiksberg, DENMARK
PA Statens Serum Institut, Copenhagen, DENMARK (non-U.S. corporation)
PI US 6641814 B1 20031104
AI US 1998-50739 19980330 (9)
PRAI DK 1997-376 19970402
US 1997-44624P 19970418 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Swartz, Rodney P
LREP Frommer Lawrence & Haug, Kowalski, Thomas J.
CLMN Number of Claims: 43
ECL Exemplary Claim: 1
DRWN 6 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 5870
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is based on the identification and characterization of a number of M. **tuberculosis** derived novel proteins and protein fragments (SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171). The invention is directed to the polypeptides and immunologically active fragments thereof, the genes encoding them, immunological compositions such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, respectively.
TI Nucleic acids fragments and polypeptide fragments derived from M. **tuberculosis**
AB The present invention is based on the identification and characterization of a number of M. **tuberculosis** derived novel proteins and protein fragments (SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, . . .
SUMM The present invention relates to a number of immunologically active, novel polypeptide fragments derived from the Mycobacterium **tuberculosis**, vaccines and other immunologic compositions containing the fragments as immunogenic components, and methods of

production and use of the polypeptides. The invention also relates to novel nucleic acid fragments derived from M. **tuberculosis** which are useful in the preparation of the polypeptide fragments of the invention or in the diagnosis of infection with M. **tuberculosis** . The invention further relates to certain fusion polypeptides, notably fusions between ESAT-6 and MPT59.

SUMM Human **tuberculosis** (hereinafter designated "TB") caused by Mycobacterium **tuberculosis** is a severe global health problem responsible for approximately 3 million deaths annually, according to the WHO. The worldwide incidence. . . has markedly changed this trend due to the advent of AIDS and the appearance of multidrug resistant strains of M. **tuberculosis**.

SUMM Immunity to M. **tuberculosis** is characterized by three basic features; i) Living bacilli efficiently induces a protective immune response in contrast to killed preparations;. . . molecule seems to be interferon gamma (INF-γ). Short term-culture filtrate (ST-CF) is a complex mixture of proteins released from M. **tuberculosis** during the first few days of growth in a liquid medium (Andersen et al., 1991). Culture filtrates has been suggested. . .

SUMM . . . invention is i.a. based on the identification and characterization of a number of previously uncharacterized culture filtrate antigens from M. **tuberculosis**. In animal models of TB, T cells mediating immunity are focused predominantly to antigens in the regions 6-12 and 17-30. . . Sanger Database (cf. below) with the genes encoding CFP21 and CFP25, (cfp25 and cfp21 respectively), shows homology to two M. **tuberculosis** DNA sequences, orf19A and orf23. The two sequences, orf19a and orf23, encode to putative proteins CFP19A and CFP23 with the. . .

SUMM The present invention is also based on the identification of a number of putative antigens from M. **tuberculosis** which are not present in Mycobacterium bovis BCG strains. The nucleotide sequences encoding these putative antigens are:

SUMM rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a, and rd1-orf9b.

SUMM . . . 152 153
RD1-ORF8 67 68
RD1-ORF2 71 72
RD1-ORF9B 69 70
RD1-ORF3 87 88
RD1-ORF9A 93 94
RD1-ORF4 89 90
RD1-ORF5 91 92
MPT59- 172
ESAT6
ESAT6- 173
MPT59

SUMM . . . in a) with respect to the ability of evoking a protective immune response against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex, or

SUMM . . . in a) with respect to the ability of evoking a protective immune response against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex,

SUMM . . . any other antigen with which it is natively associated, i.e. free of any other antigen from bacteria belonging to the **tuberculosis** complex. This can be accomplished by preparing the polypeptide fragment by means of recombinant methods in a non-mycobacterial host cell. . .

SUMM . . . and any one of 168-171 denotes any continuous stretch of at least 6 amino acid residues taken from the M. **tuberculosis** derived polypeptides in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, any one of 17-23, 42, 48,. . . being immunological equivalent thereto with respect to the ability of conferring increased resistance to infections

with bacteria belonging to the **tuberculosis** complex. Thus, included is also a polypeptide from different sources, such as other bacteria or even from eukaryotic cells.

SUMM . . . in a guinea pig and/or in a primate such as a human being against infections with bacteria belonging to the **tuberculosis** complex which is at least 20% of the acquired increased resistance conferred by Mycobacterium bovis BCG and also at least. . . other organ homogenates isolated from the mouse or guinea pig receiving a challenge infection with a virulent strain of M. **tuberculosis**, or, in a primate such as a human being, being assessed by determining the protection against development of clinical **tuberculosis** in a vaccinated group versus that observed in a control group receiving a placebo or BCG (preferably the increased resistance. . .

SUMM . . . diagnostically significant immune response in a mammal indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex; this diagnostically significant immune response can be in the form of a delayed type hypersensitivity reaction which can e.g.. . .

SUMM . . . isolated from the experimental animal which have received a challenge infection with a virulent strain of mycobacteria belonging to the **tuberculosis** complex after previously having been immunized with the polypeptide, as compared to the mycobacterial counts in a control group of experimental animals infected with the same virulent strain, which experimental animals have not previously been immunized against **tuberculosis**. The comparison of the mycobacterial counts may also be carried out with mycobacterial counts from a group of experimental animals. . .

SUMM . . . the ability of the polypeptide fragment of the invention to confer increased resistance is to compare the incidence of clinical **tuberculosis** in two groups of individuals (e.g. humans or other primates) where one group receives a vaccine as described herein which. . .

SUMM The "**tuberculosis**-complex" has its usual meaning, i.e. the complex of mycobacteria causing TB which are Mycobacterium **tuberculosis**, Mycobacterium bovis, Mycobacterium bovis BCG, and Mycobacterium africanum.

SUMM . . . other short peptide sequences), whereas the product which can be isolated from short-term culture filtrates from bacteria belonging to the **tuberculosis** complex are free of these sequences. Although it may in some applications be advantageous to produce these polypeptides recombinantly and. . .

SUMM . . . weeks of primary infection or within 4 days after the mouse has been rechallenge infected with mycobacteria belonging to the **tuberculosis** complex, the induction performed by the addition of the polypeptide to a suspension comprising about 200,000 spleen cells per ml,. . .

SUMM 3) induces an IFN-γ release from bovine PBMC derived from animals previously sensitized with mycobacteria belonging to the **tuberculosis** complex, said release being at least two times the release observed from bovine PBMC derived from animals not previously sensitized with mycobacteria belonging to the **tuberculosis** complex.

SUMM . . . as to allow for multiple expression of relevant epitopes), and an other polypeptide derived from a bacterium belonging to the **tuberculosis** complex, such as ESAT-6, MPB64, MPT64, and MPB59 or at least one T-cell epitope of any of these antigens. Other. . .

SUMM . . . first amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. **tuberculosis** protein ESAT-6 or MPT59, and a second amino acid sequence including at least one T-cell epitope derived from a M. **tuberculosis** protein different from ESAT-6 (if the first stretch of amino acids are derived from ESAT-6) or MPT59 (if the first. . .

SUMM . . . one, wherein the at least one T-cell epitope included in the second amino acid sequence is derived from a M. **tuberculosis** polypeptide (the "parent" polypeptide) selected from the group consisting of a polypeptide fragment according to the present invention and described. . . detail above and in the examples, or the amino acid sequence could be derived from any one of the M.

tuberculosis proteins DnaK, GroEL, urease, glutamine synthetase, the proline rich complex, L-alanine dehydrogenase, phosphate binding protein, Ag 85 complex, HBHA (heparin. . .

SUMM isolating the polypeptide from whole mycobacteria of the **tuberculosis** complex or from lysates or fractions thereof, e.g. cell wall containing fractions, or

SUMM . . . interesting are rapid-growing mycobacteria, e.g. M. smegmatis, as these bacteria have a high degree of resemblance with mycobacteria of the **tuberculosis** complex and therefore stand a good chance of reducing the need of performing post-translational modifications of the expression product.

SUMM . . . been administered, the amount of expressed antigen being effective to confer substantially increased resistance to infections with mycobacteria of the **tuberculosis** complex in an animal, including a human being.

SUMM . . . in an immune diagnostic agent due to their extracellular presence in culture media containing metabolizing virulent mycobacteria belonging to the **tuberculosis** complex, or because of their high homologies with such extra-cellular antigens, or because of their absence in M. bovis BCG.

SUMM . . . to the invention, and solubilizing or dispersing the polypeptide in a medium for a vaccine, and optionally adding other M. **tuberculosis** antigens and/or a carrier, vehicle and/or adjuvant substance.

SUMM . . . defined above, or some but not all of the peptides may be derived from a bacterium belonging to the M. **tuberculosis** complex. In the latter example the polypeptides not necessarily fulfilling the criteria set forth above for polypeptides may either act. . .

SUMM . . . which is a vaccine for immunizing an animal, including a human being, against TB caused by mycobacteria belonging to the **tuberculosis**-complex, comprising as the effective component a microorganism, wherein one or more copies of a DNA sequence encoding a polypeptide as. . .

SUMM The invention also relates to a method of diagnosing TB caused by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis in an animal, including a human being, comprising intradermally injecting, in the animal, a polypeptide. . .

SUMM . . . pertains to a method for immunising an animal, including a human being, against TB caused by mycobacteria belonging to the **tuberculosis** complex, comprising administering to the animal the polypeptide of the invention, or a vaccine composition of the invention as described. . .

SUMM . . . gene in the mycobacterial genome has been demonstrated to have a very limited distribution in other mycobacterial strains that M. **tuberculosis**, e.g. esat-6 is absent in both BCG and the majority of mycobacterial species isolated from the environment, such as M.. . . the invention are especially well-suited for performing the diagnosis of on-going or previous infection with virulent mycobacterial strains of the **tuberculosis** complex, and it is contemplated that it will be possible to distinguish between 1) subjects (animal or human) which have. . .

SUMM . . . vitro method for diagnosing ongoing or previous sensitization in an animal or a human being with bacteria belonging to the **tuberculosis** complex, the method comprising providing a blood sample from the animal or human being, and contacting the sample from the. . .

DRWD FIG. 1: Long term memory immune mice are very efficiently protected towards an infection with M. **tuberculosis**. Mice were given a challenge of M. **tuberculosis** and spleens were isolated at different time points. Spleen lymphocytes were stimulated in vitro with ST-CF and the release of. . .

DRWD . . . directed to molecules from 6-12 and 17-38 kDa. Splenic T cells were isolated four days after the challenge with M. **tuberculosis** and stimulated in vitro with narrow molecular mass fractions of ST-CF. The release of IFN-γ was investigated

DRWD . . . MPB51 (Ohara et al., 1995) are underlined at position 780. The nucleotides given in italics are not present in M. **tuberculosis**

H37Rv.

DETD A group of efficiently protected mice was generated by infecting 8-12 weeks old female C57Bl/6j mice with 5+10.sup.4 M. **tuberculosis** i.v. After 30 days of infection the mice were subjected to 60 days of antibiotic treatment with isoniazid and were. . .

DETD . . . used this model to identify single antigens recognized by protective T cells. Memory immune mice were reinfected with 1+10.sup.6 M. **tuberculosis** i.v. and splenic lymphocytes were harvested at day 4-6 of reinfection , a time point where this population is highly. . .

DETD The recombinant λgt11 M. **tuberculosis** DNA library constructed by R. Young (Young, R. A. et al. 1985) and obtained through the World Health Organization IMMTUB. . .

DETD In order to obtain the nucleotide sequence of the gene encoding the pv-2 binding protein, the approximately 3 kb M. **tuberculosis** derived EcoRI--EcoRI fragment from AA242 was subcloned in the EcoRI site in the pBluescriptSK+(Stratagene) and used to transform E. coli. . .

DETD Similarly, to obtain the nucleotide sequence of the gene encoding the st-3 binding protein, the approximately 5 kb M. **tuberculosis** derived EcoRI-EcoRI fragment from AA226 was subcloned in the EcoRI site in the pBluescriptSK+(Stratagene) and used to transform E. coli. . .

DETD . . . sequence obtained on the insert from lambda phage AA226, a search of homology to the nucleotide sequence of the M. **tuberculosis** genome was performed in the Sanger database (Sanger Mycobacterium **tuberculosis** database):

DETD . . . in BCG are stable deletions and/or multiple mutations which do not readily revert. While physiological differences between BCG and M. **tuberculosis** and M. bovis has been noted, the attenuating mutations which arose during serial passage of the original BCG strain has. . . has been shown to have properties as a vaccine candidate (cf. PCT/DK94/00273 and PCT/DK/00270). In order to find new M. **tuberculosis** specific diagnostic antigens as well as antigens for a new vaccine against TB, the RD1 region (17.499 bp) of M. **tuberculosis** H37Rv has been analyzed for Open Reading Frames (ORF). ORFs with a minimum length of 96 bp have been predicted. . .

DETD Identification of the ORF's rd1-orf2. rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a. and rd1-orf9b.

DETD The nucleotide sequence of rd1-orf2 from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 71. The deduced amino acid sequence of RD1-ORF2 is set forth in. . .

DETD The nucleotide sequence of rd1-orf3 from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 87. The deduced amino acid sequence of RD1-ORF2 is set forth in. . .

DETD The nucleotide sequence of rd1-orf4 from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 89. The deduced amino acid sequence of RD1-ORF2 is set forth in. . .

DETD The nucleotide sequence of **rd1-orf5** from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 91. The deduced amino acid sequence of RD1-ORF2 is set forth in. . .

DETD The nucleotide sequence of rd1-orf8 from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 67. The deduced amino acid sequence of RD1-ORF2 is set forth in. . .

DETD The nucleotide sequence of rd1-orf9a from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 93. The deduced amino acid sequence of RD1-ORF2 is set forth in. . .

DETD The nucleotide sequence of rd1-orf9b from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 69. The deduced amino acid sequence of RD1-ORF2 is set forth in. . .

DETD Cloning of the ORF's rd1-orf2. rd1-orf3. rd1-orf4. **rd1-orf5**. rd1-orf8. rd1-orf9a. and rd1-orf9b

DETD The ORF's rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b were PCR cloned in the pMST24 (Theisen et al., 1995) (rd1-orf3) or the pQE32 (QIAGEN) (rd1-orf2, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b) expression vector. Preparation of oligonucleotides and PCR amplification of the rd1-orf encoding genes, was carried out as described in example 2. Chromosomal DNA from M. **tuberculosis** H37Rv was used as

template in the PCR reactions. Oligonucleotides were synthesized on the basis of the nucleotide sequence from. . .

DETD **rd1-orf5**. A BamHI site was engineered immediately 5' of the first codon of **rd1-orf5**, and a HindIII site was incorporated right after the stop codon at the 3' end. The gene **rd1-orf5** was subcloned in pQE32, giving pTO88.

DETD Purification of Recombinant RD1-ORF2, RD1-ORF3, RD1-ORF4, **RD1-ORF5**, RD1-ORF8, RD1-ORF9a and RD1-ORF9b.

DETD The nucleotide sequences of rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a, and rd1-orf9b from M. **tuberculosis** H37Rv are set forth in SEQ ID NO: 71, 87, 89, 91, 67, 93, and 69, respectively. The deduced amino acid sequences of rd1-orf2, rd1 -orf3, rd1-orf4 **rd1-orf5**, rd1-orf8, rd1-orf9a, and rd1-orf9b are set forth in SEQ ID NO: 72, 88, 90, 92, 68, 35 94, and 70,. . .

DETD . . . the Linocin M18 protein from Brevibacterium linens, a set of degenerated primers were constructed for PCR cloning of the M. **tuberculosis** gene encoding CFP29. PCR reactions were containing 10 ng of M. **tuberculosis** chromosomal DNA in 1+low salt Taq+buffer from Stratagene supplemented with 250 μM of each of the four nucleotides (Boehringer Mannheim),. . .

DETD . . . first 150 bp of this sequence was used for a homology search using the Blast program of the Sanger Mycobacterium **tuberculosis** database:

DETD (http//www.sanger.ac.uk/projects/M-**tuberculosis**/blast.sub.13 server).

DETD This program identified a Mycobacterium **tuberculosis** sequence on cosmid cy444 in the database that is nearly 100% identical to the 150 bp sequence of the CFP29. . .

DETD . . . sequence from each of the proteins were used for a homology search using the blast program of the Sanger Mycobacterium **tuberculosis** database:

DETD . . . protein purified from culture filtrate starts at amino acid 8 and therefore the length of the protein occurring in M. **tuberculosis** culture filtrate is 175 amino acids. This gives a theoretical molecular weigh at 18517 Da and a pI at 6.8.. . .

DETD PCR reactions contained 10 ng of M. **tuberculosis** chromosomal DNA in 1+low salt Taq+buffer from Stratagene supplemented with 250 mM of each of the four nucleotides (Boehringer Mannheim),. . .

DETD . . . sequence from each of the proteins was used for a homology search using the blast program of the Sanger Mycobacterium **tuberculosis** database:

DETD http://www.sanger.ac.uk/projects/m-**tuberculosis** /TB-blast-server.

DETD . . . were found in the Sanger database. This could be due to the fact that only approximately 70% of the M. **tuberculosis** genome had been sequenced when the searches were performed. The genes encoding these proteins could be contained in the remaining. . . .

DETD . . . CFP25, EXAMPLE 3) belong to a family of fungal cutinase homologs. Among the most homologous sequences were also two Mycobacterium **tuberculosis** sequences found on cosmid MTCY13E12. The first, MTCY13E12.04 has 46% and 50% identity to CFP25 and CFP21 respectively. The second,. . .

DETD CFP25A: CFP25A has 95% identity in a 241 aa overlap to a putative M. **tuberculosis** thymidylate synthase (450 aa accession No p28176).

DETD PCR reactions contained 10 ng of M. **tuberculosis** chromosomal DNA in 1+low salt Taq+buffer from Stratagene supplemented with 250 mM of each of the four nucleotides (Boehringer Mannheim),. . .

DETD . . . sequence from each of the proteins was used for a homology search using the blast program of the Sanger Mycobacterium **tuberculosis** genome database:

DETD http//www.sanger.ac.uk/projects/m-**tuberculosis** /TB-blast-server.

DETD PCR reactions contained 10 ng of M. **tuberculosis** chromosomal DNA in 1+low salt Taq+buffer from Stratagene supplemented with 250 mM of each of the four nucleotides (Boehringer Mannheim),. . .

DETD . . . were used for the preparation and handling of DNA (Sambrook et al., 1989). The gene mpt51 was cloned from M. **tuberculosis**

H37Rv chromosomal DNA by the use of the polymerase chain reactions (PCR) technology as described previously (Oettinger and Andersen, 1994).. .

.

DETD The nucleotide sequence of the cloned 952 bp M. **tuberculosis** H37Rv PCR fragment, pTO52, containing the Shine Dalgarno sequence, the signal peptide sequence and the structural gene of MPT51, and. . .

DETD . . . the N-terminal region of the mature protein at position 144. Therefore, a structural gene encoding MPT51, mpt51, derived from M. **tuberculosis** H37Rv was found to be located at position 144-945 of the sequence shown in FIG. 5. The nucleotide sequence of. . .

DETD . . . compared to the strong recognition of the antigen that has been found during the recall of memory immunity to M. **tuberculosis**. ESAT-6 has been found in ST-CF in a truncated version were amino acids 1-15 have been deleted. The deletion includes. . .

DETD PCR reactions contained 10 ng of M. **tuberculosis** chromosomal DNA in 1+low salt Taq+buffer from Stratagene supplemented with 250 mM of each of the four nucleotides (Boehringer Mannheim),. . .

DETD

TABLE 5

IFN-γ release from splenic memory effector cells from C57BL/6J mice isolated after reinfection with M. **tuberculosis** after stimulation with
native antigens.
Antigen.sup.a IFN-γ (pg/ml).sup.b

ST-CF 12564
CFP7 .sup. ND.sup.d
CFP9 ND
CFP17 9251
CFP20 2388
CFP21 10732

. . .

DETD The skin test activity of the purified proteins was tested in M. **tuberculosis** infected guinea pigs.

DETD 1 group of guinea pigs was infected via an ear vein with 1+10.sup.4 CFU of M. **tuberculosis** H37Rv in 0,2 ml PBS. After 4 weeks skin tests were performed and 24 hours after injection erythema diameter was. . .

DETD

TABLE 6

DTH erythema diameter in guinea pigs infected with 1 + 10.sup.4 CFU of M. **tuberculosis**, after stimulation with native antigens.
Antigen.sup.a Skin reaction (mm).sup.b

Control 2.00
PPD.sup.c 15.40 (0.53)
CFP7 ND.sup.e
CFP9 ND
CFP17 11.25. . .

DETD

TABLE 6a

DTH erythema diameter of recombinant antigens in outbred guinea pigs infected with 1 + 10.sup.4 CFU of M. **Tuberculosis**.
Antigen.sup.a Skin reaction (mm).sup.b

Control 2.9 (0.3)
PPD.sup.c 14.5 (1.0)
CFP 7a 13.6 (1.4)
CFP 17 6.8 (1.9)
CFP 20. . .

DETD . . . and A.SW(H-2.sup.s) mice (Bomholtegaard, Ry) were given intravenous infections via the lateral tail vein with an inoculum of 5+10.sup.4 M. **tuberculosis** suspended in PBS in a vol. of 0.1 ml. 14 days postinfection the animals were sacrificed and spleen cells were. . .

DETD . . . female C57BL/6j(H-2.sup.b) mice (Bomholtegaard, Ry) were given intravenous infections via the lateral tail vein with an inoculum of 5+10.sup.4 M. **tuberculosis** suspended in PBS in a vol. of 0.1 ml. After 1 month of infection the mice were treated with isoniazid. . .

DETD . . . +++ +
rCFP29 +++ +++ +++ ++
rMPT51 + - - -

Mouse IFN-γ release during recall of memory immunity to M. **tuberculosis**.
-: no response; +: 1/3 of ST-CF; ++: 2/3 of ST-CF; +++: level of ST-CF.
DETD . . . rCFP21 +++
rCFP22 -
rCFP29 +
rCFP25 +++
rMPT51 +

Mouse IFN-γ release 14 days after primary infection with M. **tuberculosis**.
-: no response; +: 1/3 of ST-CF; ++: 2/3 of ST-CF; +++: level of ST-CF.
DETD . . . donors with no known exposure to patients with TB and from patients with culture or microscopy proven infection with Mycobacterium **tuberculosis**. Blood samples were drawn from the TB patients 1-4 months after diagnosis.
DETD 6 weeks after the last immunization the mice were aerosol challenged with 5+10.sup.6 viable Mycobacterium **tuberculosis**/ml. After 6 weeks of infection the mice were killed and the number of viable bacteria in lung and spleen of. . .
DETD Species Distribution of cfp7, cfp9, mpt51, rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b as well as of cfp7a, cfp7b, cfp10a, cfp17, cfp20, cfp21, cfp22, cfp22a, cfp23, cfp25 and cfp25a
DETD Presence of cfp7, cfp9, mpt51, rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b in Different Mycobacterial Species
DETD In order to determine the distribution of the cfp7, cfp9, mpt51, rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b genes in species belonging to the M. **tuberculosis**-complex and in other mycobacteria PCR and/or Southern blotting was used. The bacterial strains used are listed in TABLE 10. Genomic. . .
DETD . . . were used in order to determine the distribution of the cfp7, cfp9 and mpt51 gene in species belonging to the **tuberculosis**-complex and in other mycobacteria. The bacterial strains used are listed in TABLE 10. PCR was performed on genomic DNA prepared. . .
DETD
TABLE 10

Mycobacterial strains used in this Example.
Species and strain(s) Source

1. M. **tuberculosis** H37R v
ATCC.sup.a
(ATCC
27294)
2. H37R
aATCC
(ATCC
25177)
3. Erdman Obtained from A. Lazlo,
Ottawa, Canada
4.. . .
DETD . . . United Kingdom) with a vacuum transfer device (Milliblot, TM-v; Millipore Corp., Bedford, Mass.). The cfp7, cfp9, mpt51, rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b gene fragments were amplified by PCR from the plasmids pRVN01, pRVN02, pTO52, pTO87, pTO88, pT089, pT090,. . .

DETD cfp7, cfp9 and mpt51 were found in the M. **tuberculosis** complex including BCG and the environmental mycobacteria; M. avium, M. kansasii, M. marinum M. intracellular and M. flavescens. cfp9 was. . .

DETD There is a strong band at around 26 kDa in M. **tuberculosis** H37Rv, Ra, Erdman, M. bovis AN5, M. bovis BCG substrain Danish 1331 and M. africanum. No band was seen in. . .

DETD

TABLE 13a

Interspecies analysis of the rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b genes by Southern blotting.

Species and strain	rd1-orf2	rd1-orf3	rd1-orf4	**rd1-orf5**	rd1-orf8	rd1-orf9a	rd1-orf9b
1. M. tub. H37Rv	+	+	+	+	+	+	+
2. M. bovis	+	+	+	N.D..	.	.	

DETD Positive results for rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b were only obtained when using genomic DNA from M. **tuberculosis** and M. bovis, and not from M. bovis BCG or other mycobacteria analyzed except rd1-orf4 which also was found in. . .

DETD Southern blotting was carried out as described for rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b, The cfp7a, cfp7b, cfp10a, cfp17, cfp20, cfp21, cfp22, cfp22a, cfp23, cfp25 and cfp25a gene fragments were. . .

DETD

GENERAL INFORMATION:

NUMBER OF SEQ ID NOs: 173

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 1

LENGTH: 381

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 1

```
ggccgccggt acctatgtgg ccgccgatgc tgcggacgcg tcgacctata ccgggttctg     60
atcgaaccct gctgaccgag aggacttgtg atgtcgcaaa tcatgtacaa ctaccccgcg    120
atgttgggtc acgccgggga tatggccgga tatgccggca cgctgcagag cttgggtgcc    180
gagatcgccg tggagcaggc. . . gccatggaag atttggtgcg ggcctatcat    300
gcgatgtcca gcacccatga agccaacacc atggcgatga tggcccgcga caccgccgaa    360
gccgccaaat ggggcggcta g                                              381
```

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 2

LENGTH: 96

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 2

```
Met Ser Gln Ile Met Tyr Asn Tyr Pro Ala Met Leu Gly His Ala Gly
  1               5                  10                  15
Asp. . . Asp Thr Ala Glu Ala Ala Lys Trp Gly Gly
                85                  90                  95
```

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 3

LENGTH: 467

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 3

```
gggtagccgg accacggctg ggcaaagatg tgcaggccgc catcaaggcg gtcaaggccg     60
gcgacggcgt cataaacccg gacggcacct tgttggcggg ccccgcggtg ctgacgcccg    120
acgagtacaa ctcccggctg gtggccgccg acccggagtc caccgcggcg ttgcccgacg    180
gcgccgggct ggtcgttctg. . . cgcacccatc    360
gcgacctcat tgccggagaa atcttggcta ccgacttcga attcgccgac ctcgccgatg    420
gtgtggccat cggcgacggc gtgcgggtaa gcatcgaaaa gacctga                  467
```

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 4

LENGTH: 108

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 4
Met Ala Ala Asp Pro Glu Ser Thr Ala Ala Leu Pro Asp Gly Ala Gly
1 5 10 15
Leu. . . Gly Asp Gly Val Arg Val Ser Ile Glu Lys Thr
100 105
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 5
LENGTH: 889
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 5
cgggtctgca cggatccggg ccgggcaggg caatcgagcc tgggatccgc tggggtgcgc 60
acatcgcgga cccgtgcgcg gtacggtcga gacagcggca cgagaaagta gtaagggcga 120
taataggcgg taaagagtag cgggaagccg gccgaacgac tcggtcagac aacgccacag 180
cggccagtga ggagcagcgg. . . ccatctccaa 780
gattcgattc ttggaggctg agggtctggt gacgccccgg cgggcctcat cggggtatcg 840
gcggttcacc gcatacgact gcgcacggct gcgattcatt ctcactgcc 889
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 6
LENGTH: 162
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 6
Met Thr Asp Met Asn Pro Asp Ile Glu Lys Asp Gln Thr Ser Asp Glu
1 5 10 15
Val. . . Gln Gly Glu Asp Asp Gly Ser Thr Gly
145 150 155 160
Gly Pro
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 7
LENGTH: 898
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 7
tcgactccgg cgccaccggg caggatcacg gtgtcgacgg ggtcgccggg gaatcccacg 60
ataaccactc ttcgcgccat gaatgccagt gttggccagg cgctggcctg gcgtccacgc 120
cacacaccgc acagattagg acacgccggc ggcgcagccc tgcccgaaag accgtgcacc 180
ggtcttggca gactgtgccc. . . 780
ggcggtaata caggtgcagg tcgtgctccc acgtgaaggc gatggcaccg tggatctgaa 840
gagcggagcc ggcgcataac acaaaggttt ccgcggtctg cgccttcgcc agcggcgc 898
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 8
LENGTH: 165
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 8
Met Ala Gln Ile Thr Leu Arg Gly Asn Ala Ile Asn Thr Val Gly Glu
1 5 10 15
Leu. . . Tyr Glu Ala Ala Leu
145 150 155 160
Ala Ala Leu Gly Ala
165
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 9
LENGTH: 1054
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 9
ataatcagct caccgttggg accgacctcg accaggggtc ctttgtgact gccgggcttg 60
acgcggacga ccacagagtc ggtcatcgcc taaggctacc gttctgacct ggggctgcgt 120
gggcgccgac gacgtgaggc acgtcatgtc tcagcggccc accgccacct cggtcgccgg 180
cagtatgtca gcatgtgcag. . . gccggatgaa atgacggtcg 960
ggcggtaatc gtttgtgttg aacgcgtaga gccgatcacc gccggggctg gtgtagacct 1020
caatgtttgt gttcgccggc agggttccgg atcc 1054
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 10
LENGTH: 217
TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 10
Met Thr Pro Arg Ser Leu Val Arg Ile Val Gly Val Val Val Ala Thr
1 5 10 15
Thr. . . 195 200 205
Ala Ala Asn Arg Leu Asp His Ala Gly
210 215
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 11
LENGTH: 949
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 11
agccgctcgc gtggggtcaa ccgggtttcc acctgctcac tcattttgcc gcctttctgt 60
gtccgggccg aggcttgcgc tcaataactc ggtcaagttc cttcacagac tgccatcact 120
ggcccgtcgg cgggctcgtt gcgggtgcgc cgcgtgcggg tttgtgttcc gggcaccggg 180
tgggggcccg cccgggcgta. . . ggccgttcaa 840
ccggacgccc tcacgccaag tccgctcacc tttggccgcg accggcgtaa ccggcagcgg 900
taagcgcatc gagcacctcc actgggtcgg tgccgagatc ccagcggga 949
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 12
LENGTH: 182
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 12
Met Ala Asp Cys Asp Ser Val Thr Asn Ser Pro Leu Ala Thr Ala Thr
1 5 10 15
Ala. . . Pro Val Val Ile
165 170 175
Glu Ser Ile Thr Ile Ser
180
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 13
LENGTH: 1060
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 13
tggaccttca ccggcggtcc cttcgcttcg ggggcgacac ctaacatact ggtcgtcaac 60
ctaccgcgac accgctggga ctttgtgcca ttgccggcca ctcggggccg ctgcggcctg 120
gaaaaattgg tcgggcacgg gcggccgcgg gtcgctacca tcccactgtg aatgatttac 180
tgacccgccg actgctcacc. . . tatcaagaca agaagggagt 960
aggcgatgca cgcaaaagtc ggcgactacc tcgtggtgaa gggcacaacc acggaacggc 1020
atgatcaaca tgctgagatc atcgaggtgc gctccgcaga 1060
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 14
LENGTH: 219
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 14
Met Gly Ala Ala Ala Ala Met Leu Ala Ala Val Leu Leu Leu Thr Pro
1 5 10 15
Ile. . . 205
Gln Ala Ala Asp Phe Val Ala Gly Lys Leu Gln
210 215
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 15
LENGTH: 1198
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 15
cagatgctgc gcaacatgtt tctcggcgat ccggcaggca acaccgatcg agtgcttgac 60
ttttccaccg cggtgaccgg cggactgttc ttctcaccca ccatcgactt tctcgaccat 120
ccaccgcccc taccgcaggc ggcgacgcca actctggcag ccgggtcgct atcgatcggc 180
agcttgaaag gaagcccccg. . . 1080
ggcctggaag acggtgcggg ctaggcggcg tttgaggcag cgtagtgctg cgcgtttggt 1140
tttcccggcg tcttgcagcc tttggtagta ggcctggccc cggctgtcgg tcatccgg 1198
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 16

LENGTH: 265
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 16
Met Asn Asn Leu Tyr Arg Asp Leu Ala Pro Val Thr Glu Ala Ala Trp
1 5 10 15
Ala. . . 245 250 255
Ala Glu Ala Ser Val Ala Leu Ser His
260 265
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 17
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: VARIANT
LOCATION: (1)
OTHER INFORMATION: Ala is Ala or Ser
SEQUENCE: 17
Ala Glu Leu Asp Ala Pro Ala Gln Ala Gly Thr Glu Xaa Ala Val
1 5 10 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 18
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 18
Ala Gln Ile Thr Leu Arg Gly Asn Ala Ile Asn Thr Val Gly Glu
1 5 10 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 19
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: UNSURE
LOCATION: (3)
OTHER INFORMATION: Xaa is unknown
SEQUENCE: 19
Asp Pro Xaa Ser Asp Ile Ala Val Val Phe Ala Arg Gly Thr His
1 5 10 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 20
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 20
Thr Asn Ser Pro Leu Ala Thr Ala Thr Ala Thr Leu His Thr Asn
1 5 10 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 21
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: UNSURE
LOCATION: (2)
OTHER INFORMATION: Xaa is unknown
SEQUENCE: 21
Ala Xaa Pro Asp Ala Glu Val Val Phe Ala Arg Gly Arg Phe Glu
1 5 10 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 22
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: UNSURE

LOCATION: (1)
OTHER INFORMATION: Xaa is unknown
SEQUENCE: 22
Xaa Ile Gln Lys Ser Leu Glu Leu Ile Val Val Thr Ala Asp Glu
1 5 10 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 23
LENGTH: 19
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 23
Met Asn Asn Leu Tyr Arg Asp Leu Ala Pro Val Thr Glu Ala Ala Trp
1 5 10 15
Ala Glu Ile
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 24
LENGTH: 34
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 24
cccggctcga gaacctstac cgcgacctsg cscc 34
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 25
LENGTH: 37
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 25
gggccggatc cgasgcsgcg tccttsacsg gytgcca 37
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 26
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 26
ggaagcccca tatgaacaat ctctaccg 28
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 27
LENGTH: 32
TYPE: DNA
ORGANISM:
DETD Mycobacterium **tuberculosis**
SEQUENCE: 27
cgcgctcagc ccttagtgac tgagcgcgac cg 32
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 28
LENGTH: 24
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 28
ctcgaattcg ccgggtgcac acag 24
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 29
LENGTH: 25
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 29
ctcgaattcg cccccatacg agaac 25
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 30
LENGTH: 15
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 30
gtgtatctgc tggac 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 31
LENGTH: 15
TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 31
ccgactggct ggccg 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 32
LENGTH: 24
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 32
gaggaattcg cttagcggat cgca 24
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 33
LENGTH: 15
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 33
cccacattcc gttgg 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 34
LENGTH: 15
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 34
gtccagcaga tacac 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 35
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 35
gtacgagaat tcatgtcgca aatcatg 27
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 36
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 36
gtacgagaat tcgagcttgg ggtgccg 27
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 37
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 37
cgattccaag cttgtggccg ccgacccg 28
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 38
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 38
cgttagggat cctcatcgcc atggtgttgg 30
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 39
LENGTH: 26
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 39
cgttagggat ccggttccac tgtgcc 26
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 40
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 40
cgttagggat cctcaggtct tttcgatg 28
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 41

LENGTH: 952
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 41
gaattcgccg ggtgcacaca gccttacacg acggaggtgg acacatgaag ggtcggtcgg 60
cgctgctgcg ggcgctctgg attgccgcac tgtcattcgg gttgggcggt gtcgcggtag 120
ccgcggaacc caccgccaag gccgccccat acgagaacct gatggtgccg tcgccctcga 180
tgggccggga catcccggtg. . . . 840
acaacggaca cttcgacttc ccagccagcg gtgacaacgg ctggggctcg tgggcgcccc 900
agctgggcgc tatgtcgggc gatatcgtcg gtgcgatccg ctaagcgaat tc 952
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 42
LENGTH: 299
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 42
Met Lys Gly Arg Ser Ala Leu Leu Arg Ala Leu Trp Ile Ala Ala Leu
1 5 10 15
Ser. . . 285
Ala Met Ser Gly Asp Ile Val Gly Ala Ile Arg
290 295
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 43
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 43
gcaacacccg ggatgtcgca aatcatg 27
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 44
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 44
gtaacacccg gggtggccgc cgacccg 27
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 45
LENGTH: 37
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 45
ctactaagct tggatcccta gccgccccat ttggcgg 37
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 46
LENGTH: 38
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 46
ctactaagct tccatggtca ggtcttttcg atgcttac 38
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 47
LENGTH: 450
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 47
gtgccgcgct ccccagggtt cttatggttc gatatacctg agtttgatgg aagtccgatg 60
accagcagtc agcatacggc atggccgaaa agagtggggt gatgatggcc gaggatgttc 120
gcgccgagat cgtggccagc gttctcgaag tcgttgtcaa cgaaggcgat cagatcgaca 180
agggcgacgt cgtggtgctg. . . tcactcatgt ccacactcgg tgatctgctc 360
gccgaacaca cggtgctgcc gggcagcgcg gtggaccacc tgcatgcggt ggtcggggag 420
tggcagctcc ttgccgactt gtcgtttgcc 450
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 48
LENGTH: 71
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 48
Met Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val

```
  1               5                  10                  15
Val. . . Ala Gly
     50                  55                  60
Asp Leu Ile Ala Val Ile Ser
 65                  70
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 49
LENGTH: 750
TYPE: DNA
ORGANISM: Mycobacterium tuberculosis
SEQUENCE:  49
gggtacccat cgatgggttg cggttcggca ccgaggtgct aacgcacttg ctgacacact     60
gctagtcgaa aacgaggcta gtcgcaacgt cgatcacacg agaggactga ccatgacaac    120
ttcacccgac ccgtatgccg cgctgcccaa gctgccgtcc ttcagcctga cgtcaacctc    180
gatcaccgat gggcagccgc. . . cgagcagcgt tagcgcttta gctgggttgc    660
cgacgtcttg ccgagccgac cgcttcgtgc agcgagccga acccgccgtc atgcagcctg    720
cgggcaatgc cttcatggat gtccttggcc                                    750
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 50
LENGTH: 176
TYPE: PRT
ORGANISM: Mycobacterium tuberculosis
SEQUENCE:  50
Met Thr Thr Ser Pro Asp Pro Tyr Ala Ala Leu Pro Lys Leu Pro Ser
  1               5                  10                  15
Phe. . . Ala Val Ile Phe Gly Thr Tyr Glu Gln Arg
             165                 170                 175
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 51
LENGTH: 800
TYPE: DNA
ORGANISM: Mycobacterium tuberculosis
SEQUENCE:  51
tcatgaggtt catcggggtg atcccacgcc cgcagccgca ttcgggccgc tggcgagccg     60
gtgccgcacg ccgcctcacc agcctggtgg ccgccgcctt tgcggcggcc acactgttgc    120
ttacccccgc gctggcacca ccggcatcgg cgggctgccc ggatgccgag gtggtgttcg    180
cccgcggaac cggcgaacca. . . gtcgcgagca ggatctaacg cgagccgccc catagattcc
      720
ggctaagcaa cggctgcgcc gccgcccggc cacgagtgac cgccgccgac tggcacaccg    780
cttaccacgg ccttatgctg                                               800
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 52
LENGTH: 226
TYPE: PRT
ORGANISM: Mycobacterium tuberculosis
SEQUENCE:  52
Met Ile Pro Arg Pro Gln Pro His Ser Gly Arg Trp Arg Ala Gly Ala
  1               5                  10                  15
Ala. . . Asn Gln Ala Ala Arg Phe Val Ala Ser
    210                 215                 220
Arg Ile
225
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 53
LENGTH: 700
TYPE: DNA
ORGANISM: Mycobacterium tuberculosis
SEQUENCE:  53
ctaggaaagc ctttcctgag taagtattgc cttcgttgca taccgccctt tacctgcgtt     60
aatctgcatt ttatgacaga atacgaaggg cctaagacaa aattccacgc gttaatgcag    120
gaacagattc ataacgaatt cacagcggca caacaatatg tcgcgatcgc ggtttatttc    180
gacagcgaag acctgccgca. . . catcaggcgc cccgcacgct    600
gccgggggcc gcctctagat ccctggcggg gatcagcgag tggtcccgtt cgcccgcccg    660
tcttccagcc aggccttggt gcggccgggg tggtgagtac                          700
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 54
LENGTH: 181
TYPE: PRT
```

ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 54
Met Thr Glu Tyr Glu Gly Pro Lys Thr Lys Phe His Ala Leu Met Gln
1 5 10 15
Glu. . . Gly Ala Pro His Ala
165 170 175
Ala Gly Gly Arg Leu
180
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 55
LENGTH: 950
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 55
tgggctcggc actggctctc ccacggtggc gcgctgattt ctccccacgg taggcgttgc 60
gacgcatgtt cttcaccgtc tatccacagc taccgacatt tgctccggct ggatcgcggg 120
taaaattccg tcgtgaacaa tcgacccatc cgcctgctga catccggcag ggctggtttg 180
ggtgcgggcg cattgatcac. . . tctgcctgga 840
tccgtcccgc agctgcccgg gtctgtcctt cagatgcccg gcactgccgc accggctccc 900
gaatcgctgc acggtcgctg acgctttgtc agtaagccca taaaatcgcg 950
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 56
LENGTH: 262
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 56
Met Asn Asn Arg Pro Ile Arg Leu Leu Thr Ser Gly Arg Ala Gly Leu
1 5 10 15
Gly. . . Ala Pro Ala Pro
245 250 255
Glu Ser Leu His Gly Arg
260
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 57
LENGTH: 1000
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 57
cgaggagacc gacgatctgc tcgacgaaat cgacgacgtc ctcgaggaga acgccgagga 60
cttcgtccgc gcatacgtcc aaaagggcgg acagtgacct ggccgttgcc cgatcgcctg 120
tccattaatt cactctctgg aacacccgct gtagacctat cttctttcac tgacttcctg 180
cgccgccagg cgccggagtt. . . cggagagccg gattgccgaa 900
ttggcccgcg cgatcatcga aagccgttcg ggtgcggata ctttcggctc cgatggcggt 960
gagaagtgag ttttccgtat ttcatctcgc ctgagcaggc 1000
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 58
LENGTH: 291
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 58
Met Thr Trp Pro Leu Pro Asp Arg Leu Ser Ile Asn Ser Leu Ser Gly
1 5 10 15
Thr. . . Asp Thr Phe Gly Ser Asp Gly
275 280 285
Gly Glu Lys
290
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 59
LENGTH: 900
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 59
ttggcccgcg cgatcatcga aagccgttcg ggtgcggata ctttcggctc cgatggcggt 60
gagaagtgag ttttccgtat ttcatctcgc ctgagcaggc gatgcgcgag cgcagcgagt 120
tggcgcgtaa gggcattgcg cgggccaaaa gcgtggtggc gctggcctat gccggtggtg 180
tgctgttcgt cgcggagaat. . .
DETD . . . 780
gcccgcagtc tgacggcgaa tcgtcgggct gagtccgaaa gtccgacgcg tgtctgggac 840

cccgctgcga cgttaactgc gcctaacccc ggctcgacgc gtcgccggcc gtcctgactt 900
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 60
LENGTH: 248
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 60
Met Ser Phe Pro Tyr Phe Ile Ser Pro Glu Gln Ala Met Arg Glu Arg
1 5 10 15
Ser. . . Ser Pro
225 230 235 240
Gln Ser Asp Gly Glu Ser Ser Gly
245
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 61
LENGTH: 1560
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 61
gagtcattgc ctggtcggcg tcattccgta ctagtcggtt gtcggacttg acctactggg 60
tcaggccgac gagcactcga ccattagggt aggggccgtg acccactatg acgtcgtcgt 120
tctcggagcc ggtcccggcg ggtatgtcgc ggcgattcgc gccgcacagc tcggcctgag 180
cactgcaatc gtcgaaccca. . . 1440
ggcgctgcag gagtgcttcc acggcctggt tggccacatg atcaatttct gagcggctca 1500
tgacgaggcg cgcgagcact gacacccccc agatcatcat gggtgccatc ggtggtgtgg 1560
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 62
LENGTH: 464
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 62
Met Thr His Tyr Asp Val Val Val Leu Gly Ala Gly Pro Gly Gly Tyr
1 5 10 15
Val. . . His Gly Leu Val Gly His Met Ile Asn Phe
450 455 460
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 63
LENGTH: 550
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 63
ggcccggctc gcggccgccc tgcaggaaaa gaaggcctgc ccaggcccag actcagccga 60
gtagtcaccc agtaccccac accaggaagg accgcccatc atggcaaagc tctccaccga 120
cgaactgctg gacgcgttca aggaaatgac cctgttggag ctctccgact tcgtcaagaa 180
gttcgaggag accttcgagg. . . gaggccgccg acgaggccaa ggccaagctg gaggccgccg
gcgccaccgt 480
caccgtcaag tagctctgcc cagcgtgttc ttttgcgtct gctcggcccg tagcgaacac 540
tgcgcccgct 550
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 64
LENGTH: 130
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 64
Met Ala Lys Leu Ser Thr Asp Glu Leu Leu Asp Ala Phe Lys Glu Met
1 5 10 15
Thr. . . Glu Ala Ala Gly Ala Thr Val Thr
115 120 125
Val Lys
130
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 65
LENGTH: 900
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 65
tgaacgccat cgggtccaac gaacgcagcg ctacctgatc accaccgggt ctgttagggc 60
tcttccccag gtcgtacagt cgggccatgg ccattgaggt ttcggtgttg cgggttttca 120

ccgattcaga cgggaatttc ggtaatccgc tgggggtgat caacgccagc aaggtcgaac 180
accgcgacag gcagcagctg. . . 780
ctcagcgctg ccgatgcaac acggcggcaa ggtgatcctg caggggttgc ccgaccgcgc 840
gcatctgcaa cgagtacgaa agctcgtcgc cgtcgatgcg gtaggaacgg tcaagggcgg 900
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 66
LENGTH: 228
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 66
Met Ala Ile Glu Val Ser Val Leu Arg Val Phe Thr Asp Ser Asp Gly
1 5 10 15
Asn. . . Arg Val Val Ser Asp Gly Val
210 215 220
Ala Gln Leu Asp
225
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 67
LENGTH: 500
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 67
gtttgtggtg tcggtggtct ggggggcgcc aactgggatt cggttggggt gggtgcaggt 60
ccggcgatgg gcatcggagg tgtgggtggt ttgggtgggg ccggttcggg tccggcgatg 120
ggcatggggg gtgtgggtgg tttgggtggg gccggttcgg gtccggcgat gggcatgggg 180
ggtgtgggtg gtttagatgc. . . aaacgaagca ctggggtcga agaacggctg cgctgccata
420
tcgtccggag cttccatacc ttcgtgcggc cggaagagct tgtcgtagtc ggccgccatg 480
acaacctctc agagtgcgct 500
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 68
LENGTH: 139
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 68
Met Gly Ala Gly Pro Ala Met Gly Ile Gly Gly Val Gly Gly Leu Gly
1 5 10 15
Gly. . . 125
Ser Ile Pro Ser Cys Gly Arg Lys Ser Leu Ser
130 135
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 69
LENGTH: 2050
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 69
agcgcactct gagaggttgt catggcggcc gactacgaca agctcttccg gccgcacgaa 60
ggtatggaag ctccggacga tatggcagcg cagccgttct tcgaccccag tgcttcgttt 120
ccgccggcgc ccgcatcggc aaacctaccg aagcccaacg gccagactcc gcccccgacg 180
tccgacgacc tgtcggagcg. . . cactcgactt gctcgaccct atctacaagc gcaaggtcct
cgaattggcc 1980
gcagcgctat ccgacgattt cgagagggct ggacgtcgtt gagcgcacct gctgttgctg 2040
ctggtcctac 2050
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 70
LENGTH: 666
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 70
Met Ala Ala Asp Tyr Asp Lys Leu Phe Arg Pro His Glu Gly Met Glu
1 5 10 15
Ala. . . 650 655
Ser Asp Asp Phe Glu Arg Ala Gly Arg Arg
660 665
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 71
LENGTH: 1890
TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 71
gcagcgatga ggaggagcgg cgccaacggc ccgcgccggc gacgatgcaa agcgcagcga 60
tgaggaggag cggcgcgcat gactgctgaa ccggaagtac ggacgctgcg cgaggttgtg 120
ctggaccagc tcggcactgc tgaatcgcgt gcgtacaaga tgtggctgcc gccgttgacc 180
aatccggtcc cgctcaacga. . .
DETD . . . tcgccagacg gcaaagaggt catccaggcc 1800
ccctacatcg agcctccaga agaagtgttc gcagcacccc caagcgccgg ttaagattat 1860
ttcattgccg gtgtagcagg acccgagctc 1890
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 72
LENGTH: 591
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 72
Met Thr Ala Glu Pro Glu Val Arg Thr Leu Arg Glu Val Val Leu Asp
1 5 10 15
Gln. . . Glu Val Phe Ala Ala Pro Pro Ser Ala Gly
580 585 590
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 73
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 73
Asp Pro Val Asp Asp Ala Phe Ile Ala Lys Leu Asn Thr Ala Gly
1 5 10 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 74
LENGTH: 14
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: UNSURE
LOCATION: (14)
OTHER INFORMATION: Xaa is unknown
SEQUENCE: 74
Asp Pro Val Asp Ala Ile Ile Asn Leu Asp Asn Tyr Gly Xaa
1 5 10
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 75
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: UNSURE
LOCATION: (5)
OTHER INFORMATION: Xaa is unknown
SEQUENCE: 75
Ala Glu Met Lys Xaa Phe Lys Asn Ala Ile Val Gln Glu Ile Asp
1 5 10 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 76
LENGTH: 14
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: VARIANT
LOCATION: (3)
OTHER INFORMATION: Ala is Ala or Gln
SEQUENCE: 76
Val Ile Ala Gly Met Val Thr His Ile His Xaa Val Ala Gly
1 5 10
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 77
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 77
Thr Asn Ile Val Val Leu Ile Lys Gln Val Pro Asp Thr Trp Ser
1 5 10 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 78
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 78
Ala Ile Glu Val Ser Val Leu Arg Val Phe Thr Asp Ser Asp Gly
1 5 10 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 79
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 79
Ala Lys Leu Ser Thr Asp Glu Leu Leu Asp Ala Phe Lys Glu Met
1 5 10 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 80
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: VARIANT
LOCATION: (4)
OTHER INFORMATION: Asp is Asp or Glu
SEQUENCE: 80
Asp Pro Ala Asp Ala Pro Asp Val Pro Thr Ala Ala Gln Leu Thr
1 5 10 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 81
LENGTH: 50
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 81
Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val
1 5 10 15
Val . . Val Leu Ala Glu Ala Ala Gly Thr
35 40 45
Val Ser
50
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 82
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 82
Thr Thr Ser Pro Asp Pro Tyr Ala Ala Leu Pro Lys Leu Pro Ser
1 5 10 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 83
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 83
Thr Glu Tyr Glu Gly Pro Lys Thr Lys Phe His Ala Leu Met Gln
1 5 10 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 84
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 84
Thr Thr Ile Val Ala Leu Lys Tyr Pro Gly Gly Val Val Met Ala
1 5 10 15
SEQUENCE CHARACTERISTICS:

SEQ ID NO: 85
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: UNSURE
LOCATION: (10)
OTHER INFORMATION: Xaa is unknown
SEQUENCE: 85
Ser Phe Pro Tyr Phe Ile Ser Pro Glu Xaa Ala Met Arg Glu Xaa
1 5 10 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 86
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 86
Thr His Tyr Asp Val Val Val Leu Gly Ala Gly Pro Gly Gly Tyr
1 5 10 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 87
LENGTH: 450
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 87
agcccggtaa tcgagttcgg gcaatgctga ccatcgggtt tgtttccggc tataaccgaa 60
cggtttgtgt acgggataca aatacaggga gggaagaagt aggcaaatgg aaaaaatgtc 120
acatgatccg atcgctgccg acattggcac gcaagtgagc gacaacgctc tgcacggcgt 180
gacggccggc tcgacggcgc. . . gggcgaagcg gtccaggacg tcgcccgcac 360
ctattcgcaa atcgacgacg gcgccgccgg cgtcttcgcc taataggccc ccaacacatc 420
ggagggagtg atcaccatgc tgtggcacgc 450
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 88
LENGTH: 98
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 88
Met Glu Lys Met Ser His Asp Pro Ile Ala Ala Asp Ile Gly Thr Gln
1 5 10 15
Val. . . Gln Ile Asp Asp Gly Ala Ala Gly Val
85 90 95
Phe Ala
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 89
LENGTH: 460
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 89
gcaaccggct tttcgatcag ctgagacatc agcggcgtgc gggtcaacga cccacctgcg 60
ccaggtagcg actccgcgcg cagcaggccc gcgcccgcgc tggggcctga tccaccagcc 120
agcggatggt tcgacagcgg actggtgccg agcaggccca tctgcgcggc ttcctcgtcg 180
gctgggttgc cgccgccggt. . . gggagggcat tccgaagatc 360
gggttcgtcg tgctctggct cgcgccggga tcaaggatcg acgccatcgg ctcgagcttc 420
tcgaaaagcg tgttaaccgc ggtctcggcc tggtagacct 460
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 90
LENGTH: 139
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 90
Met Arg Val Asn Asp Pro Pro Ala Pro Gly Ser Asp Ser Ala Arg Ser
1 5 10 15
Arg. . . 125
Ser Lys Ser Val Leu Thr Ala Val Ser Ala Trp
130 135
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 91
LENGTH: 1200

TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 91
taataggccc ccaacacatc ggagggagtg atcaccatgc tgtggcacgc aatgccaccg 60
gagctaaata ccgcacggct gatggccggc gcgggtccgg ctccaatgct tgcggcggcc 120
gcgggatggc agacgctttc ggcggctctg gacgctcagg ccgtcgagtt gaccgcgcgc 180
ctgaactctc tgggagaagc. . . 1080
ccgctcgcgc aggagcgtga agaagacgac gaggacgact gggacgaaga ggacgactgg 1140
tgagctcccg taatgacaac agacttcccg gccacccggg ccggaagact tgccaacatt 1200
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 92
LENGTH: 371
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 92
Met Ile Thr Met Leu Trp His Ala Met Pro Pro Glu Leu Asn Thr Ala
1 5 10 15
Arg. . . Glu Asp Asp Trp Asp Glu Glu
355 360 365
Asp Asp Trp
370
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 93
LENGTH: 1000
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 93
gacgcgacac agaaatcctt aaggccggcg gccaaggggc cgaaggtgaa gaaggtgaag 60
ccccagaaac cgaaggccac gaagccgccc aaagtggtgt cgcagcgcgg ctggcgacat 120
tgggtgcatg cgttgacgcg aatcaacctg ggcctgtcac ccgacgagaa gtacgagctg 180
gacctgcacg ctcgagtccg. . . cactcgactt gctcgaccct 900
atctacaagc gcaaggtcct cgaattggcc gcagcgctat ccgacgattt cgagagggct 960
ggacgtcgtt gagcgcacct gctgttgctg ctggtcctac 1000
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 94
LENGTH: 308
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 94
Met Lys Lys Val Lys Pro Gln Lys Pro Lys Ala Thr Lys Pro Pro Lys
1 5 10 15
Val. . . Leu Ser Asp Phe Glu Arg
290 295 300
Ala Gly Arg Arg
305
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 95
LENGTH: 34
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 95
aagagtagat ctatgatggc cgaggatgtt cgcg 34
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 96
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 96
cggcgacgac ggatcctacc gcgtcgg 27
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 97
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 97
ccttgggaga tctttggacc ccggttgc 28
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 98

LENGTH: 25
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 98
gacgagatct tatgggctta ctgac 25
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 99
LENGTH: 33
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 99
ccccccagat ctgcaccacc ggcatcggcg ggc 33
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 100
LENGTH: 24
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 100
gcggcggatc cgttgcttag ccgg 24
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 101
LENGTH: 32
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 101
ccggctgaga tctatgacag aatacgaagg gc 32
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 102
LENGTH: 24
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 102
ccccgccagg gaactagagg cggc 24
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 103
LENGTH: 38
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 103
ctgccgagat ctaccaccat tgtcgcgctg aaataccc
DETD 38
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 104
LENGTH: 25
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 104
cgccatggcc ttacgcgcca actcg 25
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 105
LENGTH: 32
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 105
ggcggagatc tgtgagtttt ccgtatttca tc 32
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 106
LENGTH: 25
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 106
cgcgtcgagc catggttagg cgcag 25
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 107
LENGTH: 32
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 107

gaggaagatc tatgacaact tcacccgacc cg 32
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 108
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 108
catgaagcca tggcccgcag gctgcatg 28
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 109
LENGTH: 33
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 109
ggccgagatc tgtgacccac tatgacgtcg tcg 33
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 110
LENGTH: 36
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 110
ggcgcccatg gtcagaaatt gatcatgtgg ccaacc 36
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 111
LENGTH: 33
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 111
ccgggagatc tatggcaaag ctctccaccg acg 33
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 112
LENGTH: 32
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 112
cgctgggcag agctacttga cggtgacggt gg 32
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 113
LENGTH: 36
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 113
ggcccagatc tatggccatt gaggtttcgg tgttgc 36
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 114
LENGTH: 26
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 114
cgccgtgttg catggcagcg ctgagc 26
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 115
LENGTH: 24
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 115
ggacgttcaa gcgacacatc gccg 24
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 116
LENGTH: 24
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 116
cagcacgaac gcgccgtcga tggc 24
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 117
LENGTH: 26
TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 117
acagatctgt gacggacatg aacccg 26
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 118
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 118
ttttccatgg tcacgggccc ccggtact 28
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 119
LENGTH: 26
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 119
acagatctgt gcccatggca cagata 26
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 120
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 120
tttaagcttc taggcgccca gcgcggc 27
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 121
LENGTH: 26
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 121
acagatctgc gcatgcggat ccgtgt 26
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 122
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 122
ttttccatgg tcatccggcg tgatcgag 28
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 123
LENGTH: 26
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 123
acagatctgt aatggcagac tgtgat 26
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 124
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 124
ttttccatgg tcaggagatg gtgatcga 28
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 125
LENGTH: 26
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 125
acagatctgc cggctacccc ggtgcc 26
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 126
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 126
ttttccatgg ctattgcagc tttccggc 28
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 127

LENGTH: 50
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 127
Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val
1 5 10 15
Val . . Val Leu Ala Glu Ala Ala Gly Thr
35 40 45
Val Ser
50
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 128
LENGTH: 49
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 128
Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val
1 5 10 15
Val . . Pro Val Leu Ala Glu Ala Ala Gly Thr Val
35 40 45
Ser
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 129
LENGTH: 50
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 129
Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val
1 5 10 15
Val . . Val Leu Ala Glu Ala Ala Gly Thr
35 40 45
Val Ser
50
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 130
LENGTH: 33
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 130
ccgggagatc tatggcaaag ctctccaccg acg 33
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 131
LENGTH: 32
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 131
cgctgggcag agctacttga cggtgacggt gg 32
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 132
LENGTH: 36
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 132
ggcgccggca agcttgccat gacagagcag cagtgg 36
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 133
LENGTH: 26
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 133
cgaactcgcc ggatcccgtg tttcgc 26
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 134
LENGTH: 32
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 134
ggcaaccgcg agatctttct cccggccggg gc 32

SEQUENCE CHARACTERISTICS:
SEQ ID NO: 135
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 135
ggcaagcttg ccggcgccta acgaact 27

SEQUENCE CHARACTERISTICS:
SEQ ID NO: 136
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 136
ggacccagat ctatgacaga gcagcagtgg 30

SEQUENCE CHARACTERISTICS:
SEQ ID NO: 137
LENGTH: 47
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 137
ccggcagccc cggccgggag aaaagctttg cgaacatccc agtgacg 47

SEQUENCE CHARACTERISTICS:
SEQ ID NO: 138
LENGTH: 44
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 138
gttcgcaaag cttttctccc ggccggggct gccggtcgag tacc 44

SEQUENCE CHARACTERISTICS:
SEQ ID NO: 139
LENGTH: 20
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 139
ccttcggtgg atcccgtcag 20

SEQUENCE CHARACTERISTICS:
SEQ ID NO: 140
LENGTH: 450
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 140
tggcgctgtc accgaggaac ctgtcaatgt cgtcgagcag tactgaaccg ttccgagaaa 60
ggccagcatg aacgtcaccg tatccattcc gaccatcctg cggccccaca ccggcggcca 120
gaagagtgtc tcggccagcg gcgatacctt gggtgccgtc atcagcgacc tggaggccaa 180
ctattcgggc atttccgagc. . . cgccgtggcc ggtgggtgag cggagcacat 360
gacacgatac gactcgctgt tgcaggcctt gggcaacacg ccgctggttg gcctgcagcg 420
attgtcgcca cgctgggatg acgggcgaga 450

SEQUENCE CHARACTERISTICS:
SEQ ID NO: 141
LENGTH: 93
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 141
Met Asn Val Thr Val Ser Ile Pro Thr Ile Leu Arg Pro His Thr Gly
1 5 10 15
Gly. . . Ser Val Thr Ile Leu Pro Ala Val Ala Gly Gly
85 90

SEQUENCE CHARACTERISTICS:
SEQ ID NO: 142
LENGTH: 480
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 142
ggtgttcccg cggccggcta tgacaacagt caatgtgcat gacaagttac aggtattagg 60
tccaggttca acaaggagac aggcaacatg gcaacacgtt ttatgacgga tccgcacgcg 120
atgcgggaca tggcgggccg ttttgaggtg cacgcccaga cggtggagga cgaggctcgc 180
cggatgtggg cgtccgcgca. . . 360
tcccagcaga tcctcagcag ctaacgtcag ccgctgcagc acaatacttt tacaagcgaa 420

ggagaacagg ttcgatgacc atcaactatc agttcggtga tgtcgacgct catggcgcca 480
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 143
LENGTH: 98
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 143
Met Ala Thr Arg Phe Met Thr Asp Pro His Ala Met Arg Asp Met Ala
1 5 10 15
Gly. . . Gln Glu Gln Ala Ser Gln Gln Ile Leu
85 90 95
Ser Ser
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 144
LENGTH: 940
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 144
gccccagtcc tcgatcgcct catcgccttc accggccgcc agccgaccgc aggccacgtg 60
tccgccacct aacgaaagga tgatcatgcc caagagaagc gaatacaggc aaggcacgcc 120
gaactgggtc gaccttcaga ccaccgatca gtccgccgcc aaaaagttct acacatcgtt 180
gttcggctgg ggttacgacg. . . gatccgcagg gcgcgatctt 840
cagtgtgttg aagcccgcac cgcagcaata gggagcatcc cgggcaggcc cgccggccgg 900
cagattcgga gaatgctaga agctgccgcc ggcgccgccg 940
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 145
LENGTH: 261
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 145
Met Pro Lys Arg Ser Glu Tyr Arg Gln Gly Thr Pro Asn Trp Val Asp
1 5 10 15
Leu. . . Phe Ser Val Leu Lys
245 250 255
Pro Ala Pro Gln Gln
260
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 146
LENGTH: 280
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 146
ccgaaaggcg gtgcaccgca cccagaagaa aaggaaagat cgagaaatgc cacagggaac 60
tgtgaagtgg ttcaacgcgg agaaggggtt cggctttatc gcccccgaag acggttccgc 120
ggatgtattt gtccactaca cggagatcca gggaacgggc ttccgcaccc ttgaagaaaa 180
ccagaaggtc gagttcgaga tcggccacag ccctaagggc ccccaggcca ccggagtccg 240
ctcgctctga gttacccccg cgagcagacg caaaaagccc 280
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 147
LENGTH: 67
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 147
Met Pro Gln Gly Thr Val Lys Trp Phe Asn Ala Glu Lys Gly Phe Gly
1 5 10 15
Phe. . . Gly Pro Gln Ala Thr Gly Val
50 55 60
Arg Ser Leu
65
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 148
LENGTH: 540
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 148
atcgtgtcgt atcgagaacc ccggccggta tcagaacgcg ccagagcgca aacctttata 60
acttcgtgtc ccaaatgtga cgaccatgga ccaaggttcc tgagatgaac ctacggcgcc 120
atcagaccct gacgctgcga ctgctggcgg catccgcggg cattctcagc gccgcggcct 180

tcgccgcgcc agcacaggca. . . 420
cctcggtgat ggcagacgtc gccagcggca acctgccggc cctgccagac atgccggggc 480
tgcccgggtc ctaggcgtgc gcggctccta gccggtccct aacggatcga tcgtggatgc 540
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 149
LENGTH: 129
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 149
Met Asn Leu Arg Arg His Gln Thr Leu Thr Leu Arg Leu Leu Ala Ala
1 5 10 15
Ser. . . Ala Leu Pro Asp Met Pro Gly Leu Pro Gly
115 120 125
Ser
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 150
LENGTH: 400
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 150
atagtttggg gaaggtgtcc ataaatgagg ctgtcgttga ccgcattgag cgccggtgta 60
ggcgccgtgg caatgtcgtt gaccgtcggg gccggggtcg cctccgcaga tcccgtggac 120
gcggtcatta acaccacctg caattacggg caggtagtag ctgcgctcaa cgcgacggat 180
ccgggggctg ccgcacagtt. . . aattgcaagc tgtgccgggg 300
gcggcacagt acatcggcct tgtcgagtcg gttgccggct cctgcaacaa ctattaagcc 360
catgcgggcc ccatcccgcg acccggcatc gtcgccgggg 400
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 151
LENGTH: 110
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 151
Met Arg Leu Ser Leu Thr Ala Leu Ser Ala Gly Val Gly Ala Val Ala
1 5 10 15
Met. . . Glu Ser Val Ala Gly Ser Cys Asn Asn Tyr
100 105 110
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 152
LENGTH: 990
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 152
aatagtaata tcgctgtgcg gttgcaaaac gtgtgaccga ggttccgcag tcgagcgctg 60
cgggccgcct tcgaggagga cgaaccacag tcatgacgaa catcgtggtc ctgatcaagc 120
aggtcccaga tacctggtcg gagcgcaagc tgaccgacgg cgatttcacg ctggaccgcg 180
aggccgccga cgcggtgctg. . . tggttgccca gaaaatcatc taagacatac 900
gcacctccca aagacgagag cgatataacc catggctgaa gtactggtgc tcgttgagca 960
cgctgaaggc gcgttaaaga aggtcagcgc 990
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 153
LENGTH: 266
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 153
Met Thr Asn Ile Val Val Leu Ile Lys Gln Val Pro Asp Thr Trp Ser
1 5 10 15
Glu. . . 250 255
Val Gln Tyr Leu Val Ala Gln Lys Ile Ile
260 265
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 154
LENGTH: 25
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 154
ctgagatcta tgaacctacg gcgcc 25
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 155

LENGTH: 35
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 155
ctcccatggt accctaggac ccgggcagcc ccggc 35
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 156
LENGTH: 29
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 156
ctgagatcta tgaggctgtc gttgaccgc 29
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 157
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 157
ctccccgggc ttaatagttg ttgcaggagc 30
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 158
LENGTH: 33
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 158
gcttagatct atgattttct gggcaaccag gta 33
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 159
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 159
gcttccatgg gcgaggcaca ggcgtgggaa 30
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 160
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 160
ctgagatcta gaatgccaca gggaactgtg 30
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 161
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 161
tctcccgggg gtaactcaga gcgagcggac 30
SEQUENCE CHARACTERISTICS:
SEQ
DETD ID NO: 162
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 162
ctgagatcta tgaacgtcac cgtatcc 27
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 163
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 163
tctcccgggg ctcacccacc ggccacg 27
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 164
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 164

ctgagatcta tggcaacacg ttttatgacg 30
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 165
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 165
ctccccgggt tagctgctga ggatctgcth 30
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 166
LENGTH: 31
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 166
ctgaagatct atgcccaaga gaagcgaata c 31
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 167
LENGTH: 31
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 167
cggcagctgc tagcattctc cgaatctgcc g 31
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 168
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 168
Pro Gln Gly Thr Val Lys Trp Phe Asn Ala Glu Lys Gly Phe Gly
1 5 10 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 169
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: UNSURE
LOCATION: (15)
OTHER INFORMATION: Xaa is unknown
SEQUENCE: 169
Asn Val Thr Val Ser Ile Pro Thr Ile Leu Arg Pro Xaa Xaa Xaa
1 5 10 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 170
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: VARIANT
LOCATION: (1)
OTHER INFORMATION: Thr could also be Ala
SEQUENCE: 170
Thr Arg Phe Met Thr Asp Pro His Ala Met Arg Asp Met Ala Gly
1 5 10 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 171
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 171
Pro Lys Arg Ser Glu Tyr Arg Gln Gly Thr Pro Asn Trp Val Asp
1 5 10 15
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 172
LENGTH: 404
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 172

Met Ala Thr Val Asn Arg Ser Arg His His His His His His His His
1 5 10 15
Ile. . . Ser Thr Glu Gly Asn Val Thr
385 390 395 400
Gly Met Phe Ala
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 173
LENGTH: 403
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 173
Met Ala Thr Val Asn Arg Ser Arg His His His His His His His His
1 5 10 15
Ile. . .
CLM What is claimed is:
. . . with respect to the ability of evoking a protective immune response in mice against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex, or c) consists essentially of an amino acid sequence with a sequence identity of at least 80% with SEQ.
. . with respect to the ability of evoking a protective immune response in mice against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex; wherein "sequence identity" is a measure of the degree of similarity between two amino acid sequences of equal length,. . .
. . . with respect to the ability of evoking a protective immune response in mice against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex, and "sequence identity" is a measure of the degree of similarity between two amino acid sequences of equal length,. . .
. . . with respect to the ability of evoking a protective immune response in mice against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex, and "sequence identity" is a measure of the degree of similarity between two amino acid sequences of equal length,. . .
. . . with respect to the ability of evoking a protective immune response in mice against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex.

. . . weeks of primary infection or within 4 days after the mouse has been re-challenge infected with mycobacteria belonging to the **tuberculosis** complex, the induction performed by the addition of the polypeptide to a suspension comprising about 200,000 spleen cells per ml,. . .
. . . with respect to the ability of evoking a protective immune in mice response against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex, and "sequence identity" is a measure of the degree of similarity between two amino acid sequences of equal length,. . .
. . . with respect to the ability of evoking a protective immune response in mice against infections with mycobacteria belonging to the

tuberculosis complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex, and "sequence identity" is a measure of the degree of similarity between two amino acid sequences of equal length,. . .

. . . with respect to the ability of evoking a protective immune response in mice against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex.

. . . with respect to the ability of evoking a protective immune response in mice against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex.

. . . with respect to the ability of evoking a protective immune response in mice against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex.

. . . with respect to the ability of evoking a protective immune response in mice against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex.

. . . weeks of primary infection or within 4 days after the mouse has been re-challenge infected with mycobacteria belonging to the **tuberculosis** complex, the induction performed by the addition of the polypeptide to a suspension comprising about 200,000 spleen cells per ml,. . . suspension; and/or c) induces an IFN-γ release from bovine PBMC derived from animals previously sensitized with mycobacteria belonging to the **tuberculosis** complex, said release being at least two times the release observed from bovine PBMC derived from animals not previously sensitized with mycobacteria belonging to the **tuberculosis** complex.

32. A composition for diagnosing **tuberculosis** in an animal, including a human being, comprising a polypeptide according to any one of claims 1 or 2 optionally. . .
43. A composition for diagnosing **tuberculosis** in an animal, including a human being, comprising a polypeptide according to any one of claims 3 or 4 optionally. . .

L13 ANSWER 8 OF 10 USPATFULL on STN
AN 2002:314395 USPATFULL
TI Hybrids of M. **tuberculosis** antigens
IN Andersen, Peter, Bronshoj, DENMARK
Olsen, Anja Weinreich, Soborg, DENMARK
Skjot, Rikke Louise Vinther, Hedehusene, DENMARK
Rasmussen, Peter Birk, Frederiksberg, DENMARK
PI US 2002176867 A1 20021128
AI US 2001-805427 A1 20010313 (9)
RLI Continuation-in-part of Ser. No. US 1998-246191, filed on 30 Dec 1998, ABANDONED
PRAI DK 1997-1277 19971110
US 1998-70488P 19980105 (60)
US 1997-44624P 19970418 (60)
DT Utility
FS APPLICATION

LREP Thomas J. Kowalski, c/o FROMMER LAWRENCE & HAUG LLP, 745 Fifth Avenue, New York, NY, 10151
CLMN Number of Claims: 25
ECL Exemplary Claim: 1
DRWN 10 Drawing Page(s)
LN.CNT 2157
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention discloses fusion proteins of the immunodominant antigens ESAT-6 and Ag85B from Mycobacterium **tuberculosis** or homologues thereof, and a **tuberculosis** vaccine based on the fusion proteins, which vaccine induces efficient immunological memory.
TI Hybrids of M. **tuberculosis** antigens
AB The present invention discloses fusion proteins of the immunodominant antigens ESAT-6 and Ag85B from Mycobacterium **tuberculosis** or homologues thereof, and a **tuberculosis** vaccine based on the fusion proteins, which vaccine induces efficient immunological memory.
SUMM [0003] The present application discloses new fusion proteins of the immunodominant antigens ESAT-6 and Ag85B from Mycobacterium **tuberculosis** or homologues thereof, and a **tuberculosis** subunit vaccine comprising at least one fusion protein. The vaccine induced efficient immunological memory.
SUMM [0004] Human **tuberculosis** caused by Mycobacterium **tuberculosis** (M. **tuberculosis**) is a severe global health problem, responsible for approx. 3 million deaths annually, according to the WHO. The worldwide incidence of new **tuberculosis** (TB) cases had been falling during the 1960s and 1970s but during recent years this trend has markedly changed in part due to the advent of AIDS and the appearance of multidrug resistant strains of M. **tuberculosis**.
SUMM [0007] Immunity to M. **tuberculosis** is characterized by some basic features; specifically sensitized T lymphocytes mediates protection, and the most important mediator molecule seems to. . .
SUMM [0008] M. **tuberculosis** holds, as well as secretes, several proteins of potential relevance for the generation of a new TB vaccine. For a. . .
SUMM [0009] Animal **tuberculosis** is caused by Mycobacterium bovis, which is closely related to M. **tuberculosis** and within the **tuberculosis** complex. M. bovis is an important pathogen that can infect a range of hosts, including cattle and humans. **Tuberculosis** in cattle is a major cause of economic loss and represents a significant cause of zoonotic infection. A number of. . .
SUMM . . . A. D. et al 1995), genetic immunization (Huygen et al 1996, Tascon et al 1996) and attenuated strains of M. **tuberculosis** (Guleria et al 1996) are currently being explored in many laboratories. Due to the complexity of the host immune response against **tuberculosis** and the genetic restriction imposed by major histocompatibility complex molecules (MHC), it has become clear that an effective subunit vaccine. . .
SUMM . . . a significant level of anti-TB protection expressed as a reduction of bacterial numbers in organs of mice challenged with M. **tuberculosis** by the aerosol or i.v route. There is a long held debate whether the bacterial load in various organs uniformly correlates with the ultimate outcome of **tuberculosis** infection, especially in animals vaccinated with experimental TB vaccines (Wiegeshaus, E. H. et al 1970, Baldwin, S. L. et al. . .
SUMM [0015] Recent international focus on TB vaccine research and the sequencing of the M. **tuberculosis** genome (Cole et al 1998) have resulted in the accelerated identification of novel mycobacterial proteins. Culture filtrates have attracted particular. . .
SUMM . . . adoptively transfer immunity to recipient mice as late as 22 weeks after vaccination with a mixture of DDA and M. **tuberculosis** culture filtrate (Andersen, P. 1994)
SUMM . . . first amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. **tuberculosis** protein ESAT-6, and a second amino acid sequence including at least one strech of amino acids constituting a T-cell epitope derived from the M. **tuberculosis** protein Ag85B and/or a stretch of amino acids which protects the first amino acid sequence

from in vivo degradation or. . .

SUMM [0025] A preferred polypeptide within the present invention is an immunogenic antigen from M. **tuberculosis**. Such antigen can for example be derived from M. **tuberculosis** and/or M. **tuberculosis** culture filtrate. Thus, a polypeptide comprising an immunogenic portion of one of the above antigens may consist entirely of the immunogenic portion, or may contain additional sequences. The additional sequences may be derived from the native M. **tuberculosis** antigen or be heterologous and such sequences may, but need not, be immunogenic.

SUMM . . . any other antigen with which it is natively associated, i.e. free of any other antigen from bacteria belonging to the **tuberculosis** complex or a virulent mycobacterium. This can be accomplished by preparing the polypeptide by means of recombinant methods in a. . .

SUMM [0028] By the term "virulent mycobacterium" is understood a bacterium capable of causing the **tuberculosis** disease in an animal or in a human being. Examples of virulent mycobacteria are M. **tuberculosis**, M. africanum, and M. bovis. Examples of relevant animals are cattle, possums, badgers and kangaroos.

SUMM [0045] In the context of providing candidate molecules for a new vaccine against **tuberculosis**, the subdominant epitopes are however as relevant as are the dominant epitopes since it has been show (Olsen et al. . .

SUMM . . . be determined by the use of T cell lines derived from an immune individual or a person infected with M. **tuberculosis** where the T cell lines have been driven with either live mycobacteria, extracts from the bacterial cell or culture filtrate. . .

SUMM [0054] In general, M. **tuberculosis** antigens, and DNA sequences encoding such antigens, may be prepared using any one of a variety of procedures. They may be purified as native proteins from the M. **tuberculosis** cell or culture filtrate by procedures such as those described above. Immunogenic antigens may also be produced recombinantly using a. . .

SUMM . . . at least one fusion partner. The fusion partner can, in order to enhance immunogenicity, be another polypeptide derived from M. **tuberculosis**, such as of a polypeptide fragment derived from a bacterium belonging to the **tuberculosis** complex, such as TB10.4, CFP10, **RD1-ORF5**, RD1-ORF2, Rv1036, MPB64, MPT64, Ag85A, MPB59, Ag85C, 19 kDa lipoprotein, MPT32 and alpha-crystallin, or at least one T-cell epitope of. . .

SUMM . . . to the invention, and solubilizing or dispersing the polypeptide in a medium for a vaccine, and optionally adding other M. **tuberculosis** antigens and/or a carrier, vehicle and/or adjuvant substance.

SUMM . . . Nature 400: 269-71). Antigens with therapeutic properties may be identified based on their ability to diminish the severity of M. **tuberculosis** infection in experimental animals or prevent reactivation of previous infection, when administered as a vaccine. The composition used for therapeutic. . .

DRWD [0080] FIG. 1. SDS-PAGE analysis of purified recombinant M. **tuberculosis** antigens. 1 μg of protein was loaded in each lane. Lane 1: molecular weight standard; Lane 2: recombinant ESAT-6; Lane. . .

DRWD . . . with the adjuvant alone were included. Ten weeks after the first vaccination, the mice received an aerosol challenge with M. **tuberculosis** Erdman and the numbers of bacteria (CFU's) were quantified in the lungs and spleens 6 weeks later. The values are. . .

DRWD [0084] FIG. 5. Dynamics of mortality in M. **tuberculosis** -infected mice. Groups of 6-12 mice were vaccinated s.c. with either protein-based vaccines or live BCG as described in the example and challenged with a standard lethal dose of 5+10.sup.5 M. **tuberculosis** H37Rv CFUs. Numbers in parentheses indicate the mean survival time (MST±SEM) in days.

DRWD [0085] FIG. 6. Body weights of guinea pigs aerosol-infected with M. **tuberculosis**. The guinea pigs were either vaccinated with BCG, Ag85B-ESAT-6, or adjuvant-control (n=6). Data are depicted in grams. *, euthanized because. . .

DRWD [0086] FIG. 7. Proliferation of M. **tuberculosis**-specific human T cell lines (A-I) with different HLA-DR types in response to ESAT-6, Ag85B and the fusion proteins. Data are. . .

DRWD [0088] FIG. 9. Mean weight loss in vaccinated and unvaccinated cynomolgous monkeys 12 weeks after intratracheal infection with M. **tuberculosis**.

DRWD . . . FIG. 10. Vaccine efficacy in vaccinated cynomolgous monkeys (n=3) compared to unvaccinated controls, 12 weeks after intratracheal infection with M. **tuberculosis**. Protection is expressed as the log of the mean difference between the number of bacteria detected in the lungs of. . .

DETD . . . compared to the strong recognition of the antigen that has been found during the recall of memory immunity to M. **tuberculosis**. ESAT-6 has been found in ST-CF in a truncated version were amino acids 1-15 have been deleted. The deletion includes. . .

DETD [0100] PCR reactions contained 10 ng of M. **tuberculosis** chromosomal DNA in 1+low salt Taq+ buffer from Stratagene supplemented with 250 mM of each of the four nucleotides (Boehringer. . .

DETD [0116] A group of efficiently protected mice was generated by infecting 8-12 weeks old female C57BI/6j mice with 5+10.sup.4 M. **tuberculosis** i.v. After 30 days of infection the mice were subjected to 60 days of antibiotic treatment with isoniazid and were. . .

DETD . . . used this model to identify single antigens recognized by protective T cells. Memory immune mice were reinfected with 1+10.sup.6 M. **tuberculosis** i.v. and splenic lymphocytes were harvested at day 4-6 of reinfection, a time point where this population is highly reactive. . .

DETD [0119] The skin test activity of the purified proteins was tested in M. **tuberculosis** infected guinea pigs.

DETD [0120] 1 group of guinea pigs was infected via an ear vein with 1+10.sup.4 CFU of M. **tuberculosis** H37Rv in 0,2 ml PBS. After 4 weeks skin tests were performed and 24 hours after injection erythema diameter was. . .

DETD . . . TB infection in different animal models.

TABLE 1

DTH erythema diameter in guinea pigs i.v. infected with 1 + 10.sup.4 CFU M. **tuberculosis**, after stimulation with 10 μg antigen.

Antigen	Mean (mm)	SEM
PBS	3.25	0.48
PPD (2TU)	10.88	1
Ag85B-ESAT6	14.75	1.5

The values. . .

DETD . . . and A.SW(H-2.sup.s) mice (Bomholtegaard, Ry) were given intravenous infections via the lateral tail vein with an inoculum of 5+10.sup.4 M. **tuberculosis** suspended in PBS in a vol. of 0.1 ml. 14 days postinfection the animals were sacrificed and spleen cells were. . .

DETD . . . female C57BLU6j(H-2.sup.b) mice (Bomholtegaard, Ry) were given intravenous infections via the lateral tail vein with an inoculum of 5+10.sup.4 M. **tuberculosis** suspended in PBS in a vol. of 0.1 ml. After 1 month of infection the mice were treated with isoniazid. . .

DETD . . . (H2.sup.k) A.SW (H2.sup.s)

Ag85B-ESAT6	+++	+++	+++	++
ESAT6-Ag85B	+++	-	+	-

Mouse IFN-γ release 14 days after primary infection with M. **tuberculosis**.

-: no response; +: 1/3 of ST-CF; ++: 2/3 of ST-CF; +++: level of ST-CF.
n.d. = not determined.
DETD [0130] Mouse IFN-γ release during recall of memory immunity to M. **tuberculosis**. -: no response; +: 1/3 of ST-CF; ++: 2/3 of ST-CF; +++: level of ST-CF.
DETD . . . donors with no known ex-posure to patients with TB and from patients with culture or microscopy proven infection with Mycobacterium **tuberculosis**. Blood samples were drawn from the TB patients 1-4 months after diagnosis.
DETD [0149] M. **tuberculosis** Erdman and H37Rv was grown at 37° C. in modified Sauton medium enriched with 0.5% sodium pyruvate and 0.5% glucose.. . .
DETD [0151] Recombinant Ag85B was produced as follows: The coding region of ag85B was amplified by PCR from M. **tuberculosis** H37Rv chromosomal DNA with the following primer sets:

OPBR-77: GTTCGCAAAGCTTTTCTCCCGGCCGGGGCTGCCGGTCGAGTACC
(SEQ ID NO:11)
HindIII
NO:11)
DETD . . . the production of recombinant Ag85B, the coding region (without the secretory signal sequence) of Ag85B was PCR amplified from M. **tuberculosis** H37Rv chromosomal DNA using Ag85B-F1 and Ag85B-R2 primers. A unique BamHI site was introduced by the Ag85B-R2 primer. The PCR. . .
DETD . . . immunization either by the aerosol route in a Glas-Col inhalation exposure system, calibrated to deliver approximately 100 CFUs of M. **tuberculosis** Erdman/lung or by the i.v. route with an inoculum of 5+10.sup.4 CFU of M. **tuberculosis** (H37Rv) suspended in PBS in a volume of 0.2 ml. Mice were sacrificed 6 weeks (aerosol route) or 2 weeks. . .
DETD . . . naive mice were included as controls. Ten weeks after the first immunization, the mice received an aerosol challenge with M. **tuberculosis** Erdman. FIG. 3 shows the number of bacteria in lungs and spleens expressed as mean log.sub.10 CFU. Even with a. . .
DETD . . . mice were challenged by the aerosol (Exp. 1 and 2) or by the i.v (Exp 3) route with virulent M. **tuberculosis**. Six (Exp. 1 and 2) or two weeks (Exp. 3) post challenge, the mice were killed and the bacterial numbers. . .
DETD . . . included naive mice, BCG-vaccinated mice and a group of mice receiving the adjuvant alone. Mice were aerosol challenged with M. **tuberculosis** Erdman 10 and 30 weeks after the first vaccination. Both the fusion protein and BCG induced significant and similar levels. . . was observed after a longer rest period (30 weeks) and both vaccines induced long-lived memory immunity, which protected efficiently against **tuberculosis**. However, whereas the subunit vaccine promoted a stable level of protective immunity over the observation period, the efficacy of BCG. . . injected three times with the experimental vaccines emulsified in MPL-DDA.
.sup.bBacterial numbers are given as mean log.sub.10 CFU of M. **tuberculosis** ± SEM (n = 5) isolated from the spleen and lung 6 weeks post aerosol challenge (Exp. 1 and Exp.. . .
DETD . . . injected three times with the experimental vaccines emulsified in MPL-DDA.
.sup.bBacterial numbers are given as mean log.sub.10 CFU of M. **tuberculosis** ± SEM (n = 4-5) isolated from the spleen and lung 6 weeks post aerosol challenge.
.sup.cIn Exp 2 the. . .
DETD [0174] M. **tuberculosis** Erdman and H37Rv were grown at 37° C. in modified Sauton medium enriched with 0.5% sodium pyruvate and 0.5% glucose. . .
DETD . . . long-term survival, mice were challenged intravenously 6 wk following the last immunization with a lethal dose of 5+105 CFU M. **tuberculosis** H37Rv. Three weeks following infection, 3 mice per group were sacrificed and CFU counts in organs were determined by plating. . .
DETD [0186] Guinea pigs were challenged 12 weeks after the initial vaccination in either a Glas-Col inhalation exposure system with M.

tuberculosis Erdman (the SSI experiment 1) or using a contained Henderson apparatus (The CAMR experiment 2) as previously described (9); Williams,. . .

DETD [0189] Protection Against Death from M. **tuberculosis** Infection in Ag85B-ESAT-6 Fusion Protein Vaccinated Mice

DETD . . . the lung at this time-point. Severe loss of body weight, or wasting, is a common and well-described clinical symptom in **tuberculosis** patients (Prout, S. et al 1980). Hence, we monitored the body weight as a potentially important parameter of M. **tuberculosis**-triggered disease in guinea pigs (FIG. 6). When the guinea pigs had lost 20% of maximum weight or, if showing other. . .

DETD . . . derived from 7 TB patients and 2 PPD-converters representing 8 different HLA-DR phenotypes. The T cell lines raised against M. **tuberculosis** were tested with respect to their ability to specifically proliferate in the presence of ESAT-6, Ag85B and the fusion protein.. . .

DETD . . . regarded positive. Responses to PBS were less than 5 mm.

.sup.cBacterial numbers are given as mean log.sub.10 CFU of M. **tuberculosis** ± SEM (n = 5-6) isolated from the spleen and lung.

.sup.dNA, not available, due to severe disease, they were. . .

DETD . . . to subsequent in vitro rechallenge of lymphocytes with the vaccine. Vaccinated animals show significant protection against aerosol infection with M. **tuberculosis** as well as reduced pathology and weight loss, see FIGS. 8-10.

DETD [0227] Patent application PA 2000 00666 (our ref. 22030 DK1) "Nucleic acid fragments and polypeptide fragments derived from M. **tuberculosis**"

DETD [0228] U.S. patent application No. 09/0505,739 "Nucleic acid fragments and polypeptide fragments derived from M. **tuberculosis**"

DETD [0229] Patent application WO 01/04151 (our ref.23388 DK1) " **Tuberculosis** vaccine and diagnostic based on the Mycobacterium **tuberculosis** esat-6 gene family".

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 1
LENGTH: 95
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 1

Met Thr Glu Gln Gln Trp Asn Phe Ala Gly Ile Glu Ala Ala Ala Ser
1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 2
LENGTH: 325
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: SIGNAL
LOCATION: (1)..(40)
SEQUENCE: 2

Met Thr Asp Val Ser Arg Lys Ile Arg Ala Trp Gly Arg Arg Leu Met
1. . .

CLM What is claimed is:

. . . first amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. **tuberculosis** protein ESAT-6, and a second amino acid sequence including at least one stretch of amino acids con-stituting a T-cell epitope derived from the M. **tuberculosis** protein Ag85B, said first and second amino acid sequences optionally being fused via a linker sequence; (b) a polypeptide comprising. . .

. . . for the preparation of a pharmaceutical composition, e.g. for the vaccination against infections caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis.

. . . to whom the vaccine has been administered, the amount of expressed antigen being effective to confer substantially increased resistance to **tuberculosis** caused by virulent mycobacteria, e.g. by

Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, in an animal, including a human being. . . . a nucleic acid fragment according to claim 12 or 13 for the preparation of a composition for the diagnosis of **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis.

. . . nucleic acid fragment according to claim 12 or 13 for the preparation of a pharmaceutical composition for the vaccination against **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis.

18. A vaccine for immunizing an animal, including a human being, against **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, comprising as the effective component a non-pathogenic microorganism, wherein at least one copy of a. . . . . the polypeptide from the host cell or culture medium; (b) isolating Ag85B and ESAT-6 from a whole mycobacterium, e.g. Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, from culture filtrate or from lysates or fractions thereof, and fusing the polypeptides; (c) synthesizing. . .

22. A method for immunising an animal, including a human being, against **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, comprising administering to the animal the polypeptide according to claim 1, the immunogenic composition according. . .

. . . first amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. **tuberculosis** protein ESAT-6, and a second amino acid sequence including at least one stretch of amino acids con-stituting a T-cell epitope derived from the M. **tuberculosis** protein Ag85B, said first and second amino acid sequences optionally being fused via a linker sequence; (b) a polypeptide comprising. . .

. . . first amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. **tuberculosis** protein ESAT-6, and a second amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. **tuberculosis** protein Ag85B, said first and second amino acid sequences optionally being fused via a linker sequence; (b) a polypeptide comprising. . .

L13 ANSWER 9 OF 10 USPATFULL on STN
AN 2002:178550 USPATFULL
TI Nucleic acid fragments and polypeptide fragments derived from M. **tuberculosis**
IN Andersen, Peter, Bronshoj, DENMARK
Nielsen, Rikke, Frederiksberg C, DENMARK
Oettinger, Thomas, Hellerup, DENMARK
Rasmussen, Peter Birk, Kobenhaven O, DENMARK
Rosenkrands, Ida, Kobenhaven O, DENMARK
Weldingh, Karin, Kobenhaven N, DENMARK
Florio, Walter, Frederiksberg C, DENMARK
PA STATENS SERUM INSTITUT (non-U.S. corporation)
PI US 2002094336 A1 20020718
AI US 2001-791171 A1 20010220 (9)
RLI Division of Ser. No. US 1998-50739, filed on 30 Mar 1998, PENDING
PRAI DK 1997-376 19970402
DK 1997-1277 19971110
US 1997-44624P 19970418 (60)
US 1998-70488P 19980105 (60)
DT Utility
FS APPLICATION
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CLMN Number of Claims: 53
ECL Exemplary Claim: 1

DRWN 6 Drawing Page(s)
LN.CNT 6134
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is based on the identification and characterization of a number of M. **tuberculosis** derived novel proteins and protein fragments (SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171). The invention is directed to the polypeptides and immunologically active fragments thereof, the genes encoding them, immunological compositions such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, respectively.

TI Nucleic acid fragments and polypeptide fragments derived from M. **tuberculosis**

AB The present invention is based on the identification and characterization of a number of M. **tuberculosis** derived novel proteins and protein fragments (SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48,. . .

SUMM [0001] The present invention relates to a number of immunologically active, novel polypeptide fragments derived from the Mycobacterium **tuberculosis**, vaccines and other immunologic compositions containing the fragments as immunogenic components, and methods of production and use of the polypeptides. The invention also relates to novel nucleic acid fragments derived from M. **tuberculosis** which are useful in the preparation of the polypeptide fragments of the invention or in the diagnosis of infection with M. **tuberculosis** . The invention further relates to certain fusion polypeptides, notably fusions between ESAT-6 and MPT59.

SUMM [0002] Human **tuberculosis** (hereinafter designated "TB") caused by Mycobacterium **tuberculosis** is a severe global health problem responsible for approximately 3 million deaths annually, according to the WHO. The worldwide incidence. . . has markedly changed this trend due to the advent of AIDS and the appearance of multidrug resistant strains of M. **tuberculosis**.

SUMM [0005] Immunity to M. **tuberculosis** is characterized by three basic features; i) Living bacilli efficiently induces a protective immune response in contrast to killed preparations;. . .

SUMM [0006] Short term-culture filtrate (ST-CF) is a complex mixture of proteins released from M. **tuberculosis** during the first few days of growth in a liquid medium (Andersen et al., 1991). Culture filtrates has been suggested. . .

SUMM . . . invention is i.a. based on the identification and characterization of a number of previously uncharacterized culture filtrate antigens from M. **tuberculosis**. In animal models of TB, T cells mediating immunity are focused predominantly to antigens in the regions 6-12 and 17-30. . . the Sanger Database (cf. below) with the genes encoding CFP21 and CFP25, (cfp25 and cfp21respectively), shows homology to two M. **tuberculosis** DNA sequences, orf19A and orf23. The two sequences, orf19a and orf23, encode to putative proteins CFP19A and CFP23 with the. . .

SUMM [0011] The present invention is also based on the identification of a number of putative antigens from M. **tuberculosis** which are not present in Mycobacterium bovis BCG strains. The nucleotide sequences encoding these putative antigens are: rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, **rd1-orf5**, rd1-orf9a, and rd1-orf9b.

SUMM . . . in a) with respect to the ability of evoking a protective immune response against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex, or

SUMM . . . in a) with respect to the ability of evoking a protective immune response against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or

ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex,

SUMM . . . any other antigen with which it is natively associated, i.e. free of any other antigen from bacteria belonging to the **tuberculosis** complex. This can be accomplished by preparing the polypeptide fragment by means of recombinant methods in a non-mycobacterial host cell. . .

SUMM . . . and any one of 168-171 denotes any continuous stretch of at least 6 amino acid residues taken from the M. **tuberculosis** derived polypeptides in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, any one of 17-23, 42, 48,. . . being immunological equivalent thereto with respect to the ability of conferring increased resistance to infections with bacteria belonging to the **tuberculosis** complex. Thus, included is also a polypeptide from different sources, such as other bacteria or even from eukaryotic cells.

SUMM . . . in a guinea pig and/or in a primate such as a human being against infections with bacteria belonging to the **tuberculosis** complex which is at least 20% of the acquired increased resistance conferred by Mycobacterium bovis BCG and also at least. . . other organ homogenates isolated from the mouse or guinea pig receiving a challenge infection with a virulent strain of M. **tuberculosis**, or, in a primate such as a human being, being assessed by determining the protection against development of clinical **tuberculosis** in a vaccinated group versus that observed in a control group receiving a placebo or BCG (preferably the increased resistance. . .

SUMM . . . diagnostically significant immune response in a mammal indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex; this diagnostically significant immune response can be in the form of a delayed type hypersensitivity reaction which can e.g.. . .

SUMM . . . isolated from the experimental animal which have received a challenge infection with a virulent strain of mycobacteria belonging to the **tuberculosis** complex after previously having been immunized with the polypeptide, as compared to the mycobacterial counts in a control group of experimental animals infected with the same virulent strain, which experimental animals have not previously been immunized against **tuberculosis**. The comparison of the mycobacterial counts may also be carried out with mycobacterial counts from a group of experimental animals. . .

SUMM . . . the ability of the polypeptide fragment of the invention to confer increased resistance is to compare the incidence of clinical **tuberculosis** in two groups of individuals (e.g. humans or other primates) where one group receives a vaccine as described herein which. . .

SUMM [0033] The "**tuberculosis**-complex" has its usual meaning, i.e. the complex of mycobacteria causing TB which are Mycobacterium **tuberculosis**, Mycobacterium bovis, Mycobacterium bovis BCG, and Mycobacterium africanum.

SUMM . . . other short peptide sequences), whereas the product which can be isolated from short-term culture filtrates from bacteria belonging to the **tuberculosis** complex are free of these sequences. Although it may in some applications be advantageous to produce these polypeptides recombinantly and. . .

SUMM . . . weeks of primary infection or within 4 days after the mouse has been rechallenge infected with mycobacteria belonging to the **tuberculosis** complex, the induction performed by the addition of the polypeptide to a suspension comprising about 200,000 spleen cells per ml,. . .

SUMM [0050] 3) induces an IFN-γ release from bovine PBMC derived from animals previously sensitized with mycobacteria belonging to the **tuberculosis** complex, said release being at least two times the release observed from bovine PBMC derived from animals not previously sensitized with mycobacteria belonging to the **tuberculosis** complex.

SUMM . . . as to allow for multiple expression of relevant epitopes), and an other polypeptide derived from a bacterium belonging to the **tuberculosis** complex, such as ESAT-6, MPB64, MPT64, and MPB59 or at least one T-cell epitope of any of these antigens. Other. . .

SUMM . . . first amino acid sequence including at least one stretch of amino acids constituting a S-cell epitope derived from the M. **tuberculosis** protein ESAT-6 or MPT59, and a second amino acid sequence including at least one T-cell epitope derived from a M. **tuberculosis** protein different from ESAT-6 (if the first stretch of amino acids are derived from ESAT-6) or MPT59 (if the first. . .

SUMM . . . one, wherein the at least one T-cell epitope included in the second amino acid sequence is derived from a M. **tuberculosis** polypeptide (the "parent" polypeptide) selected from the group consisting of a polypeptide fragment according to the present invention and described. . . detail above and in the examples, or the amino acid sequence could be derived from any one of the M. **tuberculosis** proteins DnaK, GroEL, urease, glutamine synthetase, the proline rich complex, L-alanine dehydrogenase, phosphate binding protein, Ag 85 complex, HBHA (heparin. . .

SUMM [0078] isolating the polypeptide from whole mycobacteria of the **tuberculosis** complex or from lysates or fractions thereof, e.g. cell wall containing fractions, or

SUMM . . . interesting are rapid-growing mycobacteria, e.g. M. smegmatis, as these bacteria have a high degree of resemblance with mycobacteria of the **tuberculosis** complex and therefore stand a good chance of reducing the need of performing post-translational modifications of the expression product.

SUMM . . . been administered, the amount of expressed antigen being effective to confer substantially increased resistance to infections with mycobacteria of the **tuberculosis** complex in an animal, including a human being.

SUMM . . . in an immune diagnostic agent due to their extracellular presence in culture media containing metabolizing virulent mycobacteria belonging to the **tuberculosis** complex, or because of their high homologies with such extracellular antigens, or because of their absence in M. bovis BCG.

SUMM . . . to the invention, and solubilizing or dispersing the polypeptide in a medium for a vaccine, and optionally adding other M. **tuberculosis** antigens and/or a carrier, vehicle and/or adjuvant substance.

SUMM . . . defined above, or some but not all of the peptides may be derived from a bacterium belonging to the M. **tuberculosis** complex. In the latter example the polypeptides not necessarily fulfilling the criteria set forth above for polypeptides may either act. . .

SUMM . . . which is a vaccine for immunizing an animal, including a human being, against TB caused by mycobacteria belonging to the **tuberculosis**-complex, comprising as the effective component a microorganism, wherein one or more copies of a DNA sequence encoding a polypeptide as. . .

SUMM [0116] The invention also relates to a method of diagnosing TB caused by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis in an animal, including a human being, comprising intradermally injecting, in the animal, a polypeptide. . .

SUMM . . . pertains to a method for immunising an animal, including a human being, against TB caused by mycobacteria belonging to the **tuberculosis** complex, comprising administering to the animal the polypeptide of the invention, or a vaccine composition of the invention as described. . .

SUMM . . . gene in the mycobacterial genome has been demonstrated to have a very limited distribution in other mycobacterial strains that M. **tuberculosis**, e.g. esat-6 is absent in both BCG and the majority of mycobacterial species isolated from the environment, such as M.. . . the invention are especially well-suited for performing the diagnosis of on-going or previous infection with virulent mycobacterial strains of the **tuberculosis** complex, and it is contemplated that it will be possible to distinguish between 1) subjects (animal or human) which have. . .

SUMM . . . vitro method for diagnosing ongoing or previous sensitization in an animal or a human being with bacteria belonging to the **tuberculosis** complex, the method comprising providing a blood sample from the animal or human being, and contacting the sample from

the. . .

DRWD [0128] FIG. 1: Long term memory immune mice are very efficiently protected towards an infection with M. **tuberculosis**. Mice were given a challenge of M. **tuberculosis** and spleens were isolated at different time points. Spleen lymphocytes were stimulated in vitro with ST-CF and the release of. . .

DRWD . . . directed to molecules from 6-12 and 17-38 kDa. Splenic T cells were isolated four days after the challenge with M. **tuberculosis** and stimulated in vitro with narrow molecular mass fractions of ST-CF. The release of IFN-γwas investigated

DRWD . . . MPB51 (Ohara et al., 1995) are underlined at position 780. The nucleotides given in italics are not present in M. **tuberculosis** H37Rv.

DETD [0135] A group of efficiently protected mice was generated by infecting 8-12 weeks old female C57Bl/6j mice with 5+10.sup.4 M. **tuberculosis** i.v. After 30 days of infection the mice were subjected to 60 days of antibiotic treatment with isoniazid and were. .

DETD . . . used this model to identify single antigens recognized by protective T cells. Memory immune mice were reinfected with 1+10.sup.6 M. **tuberculosis** i.v. and splenic lymphocytes were harvested at day 4-6 of reinfection, a time point where this population is highly reactive. . .

DETD [0140] The recombinant λgt11 M. **tuberculosis** DNA library constructed by R. Young (Young, R. A. et al. 1985) and obtained through the World Health Organization IMMTUB. . .

DETD . . . In order to obtain the nucleotide sequence of the gene encoding the pv-2 binding protein, the approximately 3 kb M. **tuberculosis** derived EcoRI--EcoRI fragment from AA242 was subcloned in the EcoRI site in the pBluescriptSK+(Stratagene) and used to transform E. coli. . .

DETD [0150] Similarly, to obtain the nucleotide sequence of the gene encoding the st-3 binding protein, the approximately 5 kb M. **tuberculosis** derived EcoRI--EcoRI fragment from AA226 was subcloned in the EcoRI site in the pBluescriptSK+(Stratagene) and used to transform E. coli. . .

DETD . . . sequence obtained on the insert from lambda phage AA226, a search of homology to the nucleotide sequence of the M. **tuberculosis** genome was performed in the Sanger database (Sanger Mycobacterium **tuberculosis** database):

DETD . . . in BCG are stable deletions and/or multiple mutations which do not readily revert. While physiological differences between BCG and M. **tuberculosis** and M. bovis has been noted, the attenuating mutations which arose during serial passage of the original BCG strain has. . . has been shown to have properties as a vaccine candidate (cf. PCT/DK94/00273 and PCT/DK/00270). In order to find new M. **tuberculosis** specific diagnostic antigens as well as antigens for a new vaccine against TB, the RD1 region (17.499 bp) of M. **tuberculosis** H37Rv has been analyzed for Open Reading Frames (ORF). ORFs with a minimum length of 96 bp have been predicted. . .

DETD [0177] Identification of the ORF's rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf2, rd1-orf9a, and rd1-orf9b.

DETD [0178] The nucleotide sequence of rd1-orf2 from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 71. The deduced amino acid sequence of RD1-ORF2 is set forth in. . .

DETD [0179] The nucleotide sequence of rd1-orf3 from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 87. The deduced amino acid sequence of RD1-ORF2 is set forth in. . .

DETD [0180] The nucleotide sequence of rd1-orf4 from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 89. The deduced amino acid sequence of RD1-ORF2 is set forth in. . .

DETD [0181] The nucleotide sequence of **rd1-orf5** from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 91. The deduced amino acid sequence of RD1-ORF2 is set forth in. . .

DETD [0182] The nucleotide sequence of rd1-orf8 from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 67. The deduced amino acid sequence of RD1-ORF2 is set forth in. . .

DETD [0183] The nucleotide sequence of rd1-orf9a from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 93. The deduced amino acid sequence of RD1-ORF2 is set forth in. . .

DETD [0184] The nucleotide sequence of rd1-orf9b from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 69. The deduced amino acid sequence of RD1-ORF2 is set forth in. . .

DETD [0188] The DNA sequence **rd1-orf5** (SEQ ID NO: 91) contained an open reading frame starting with a GTG codon at position 3128-3130 and ending with. . .

DETD [0192] Cloning of the ORF's rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a, and rd1-orf9b.

DETD [0193] The ORF's rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b were PCR cloned in the pMST24 (Theisen et al., 1995) (rd1-orf3) or the pQE32 (QIAGEN) (rd1-orf2, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b) expression vector. Preparation of oligonucleotides and PCR amplification of the rd1-orf encoding genes, was carried out as described in example 2. Chromosomal DNA from M. **tuberculosis** H37Rv was used as template in the PCR reactions. Oligonucleotides were synthesized on the basis of the nucleotide sequence from. . .

DETD [0200] **rd1-orf5**.

DETD [0201] A BamHI site was engineered immediately 5' of the first codon of **rd1-orf5**, and a HindIII site was incorporated right after the stop codon at the 3' end. The gene **rd1-orf5** was subcloned in pQE32, giving pTO88.

DETD [0209] Purification of recombinant RD1-ORF2, RD1-ORF3, RD1-ORF4, **RD1-ORF5**, RD1-ORF8, RD1-ORF9a and RD1-ORF9b.

DETD [0211] The nucleotide sequences of rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a, and rd1-orf9b from M. **tuberculosis** H37Rv are set forth in SEQ ID NO: 71, 87, 89, 91, 67, 93, and 69, respectively. The deduced amino acid sequences of rd1-orf2, rd1-orf3, rd1-orf4 **rd1-orf5**, rd1-orf8, rd1-orf9a, and rd1-orf9b are set forth in SEQ ID NO: 72, 88, 90, 92, 68, 94, and 70, respectively.

DETD . . . the Linocin M18 protein from Brevibacterium linens, a set of degenerated primers were constructed for PCR cloning of the M. **tuberculosis** gene encoding CFP29. PCR reactions were containing 10 ng of M. **tuberculosis** chromosomal DNA in 1+low salt Taq+ buffer from Stratagene supplemented with 250 μM of each of the four nucleotides (Boehringer. . .

DETD . . . first 150 bp of this sequence was used for a homology search using the Blast program of the Sanger Mycobacterium **tuberculosis** database:

DETD [0230] (http//www.sanger.ac.uk/projects/M-**tuberculosis** /blast_server).

DETD [0231] This program identified a Mycobacterium **tuberculosis** sequence on cosmid cy444 in the database that is nearly 100% identical to the 150 bp sequence of the CFP29. . .

DETD . . . sequence from each of the proteins were used for a homology search using the blast program of the Sanger Mycobacterium **tuberculosis** database:

DETD . . . protein purified from culture filtrate starts at amino acid 8 and therefore the length of the protein occurring in M. **tuberculosis** culture filtrate is 175 amino acids. This gives a theoretical molecular weigh at 18517 Da and a pI at 6.8.. . .

DETD . . . with gene specific primers, for recombinant expression in E. coli of the proteins. PCR reactions contained 10 ng of M. **tuberculosis** chromosomal DNA in 1+low salt Taq+ buffer from Stratagene supplemented with 250 mM of each of the four nucleotides (Boehringer. . .

DETD . . . sequence from each of the proteins was used for a homology search using the blast program of the Sanger Mycobacterium **tuberculosis** database:

DETD [0296] http: //www.sanger.ac.uk/projects/m-**tuberculosis** /TB-blast-server.

DETD . . . were found in the Sanger database. This could be due to the fact that only approximately 70% of the M. **tuberculosis** genome had been sequenced when the searches were performed. The genes encoding these proteins could be contained in the remaining. . .

DETD . . . CFP25, EXAMPLE 3) belong to a family of fungal cutinase homologs. Among the most homologous sequences were also two

Mycobacterium **tuberculosis** sequences found on cosmid MTCY13E12. The first, MTCY13E12.04 has 46% and 50% identity to CFP25 and CFP21 respectively. The second,. . .

DETD [0336] CFP25A: CFP25A has 95% identity in a 241 aa overlap to a putative M. **tuberculosis** thymidylate synthase 450 aa accession No p28176).

DETD [0343] PCR reactions contained 10 ng of M. **tuberculosis** chromosomal DNA in 1+ low salt Taq+ buffer from Stratagene supplemented with 250 mM of each of the four nucleotides. . .

DETD . . . sequence from each of the proteins was used for a homology search using the blast program of the Sanger Mycobacterium **tuberculosis** genome database:

DETD [0366] http//www.sanger.ac.uk/projects/m-**tuberculosis** /TB-blast-server.

DETD [0374] PCR reactions contained 10 ng of M. **tuberculosis** chromosomal DNA in 1+ low salt Taq+ buffer from Stratagene supplemented with 250 mM of each of the four nucleotides. . .

DETD . . . were used for the preparation and handling of DNA (Sambrook et al., 1989). The gene mpt51 was cloned from M. **tuberculosis** H37Rv chromosomal DNA by the use of the polymerase chain reactions (PCR) technology as described previously (Oettinger and Andersen, 1994).. . .

DETD [0392] The nucleotide sequence of the cloned 952 bp M. **tuberculosis** H37Rv PCR fragment, pTO52, containing the Shine Dalgarno sequence, the signal peptide sequence and the structural gene of MPT51, and. . .

DETD . . . the N-terminal region of the mature protein at position 144. Therefore, a structural gene encoding MPT51, mpt51, derived from M. **tuberculosis** H37Rv was found to be located at position 144-945 of the sequence shown in FIG. 5. The nucleotide sequence of. . .

DETD . . . compared to the strong recognition of the antigen that has been found during the recall of memory immunity to M. **tuberculosis**. ESAT-6 has been found in ST-CF in a truncated version were amino acids 1-15 have been deleted. The deletion includes. . .

DETD [0415] PCR reactions contained 10 ng of M. **tuberculosis** chromosomal DNA in 1+ low salt Taq+ buffer from Stratagene supplemented with 250 mM of each of the four nucleotides. . .

DETD . . . same high level as ST-CF.

TABLE 5

IFN-γ release from splenic memory effector cells from C57BL/6J mice isolated after reinfection with M. **tuberculosis** after stimulation with native antigens.

Antigen.sup.a	IFN-γ (pg/ml).sup.b
ST-CF	12564
CFP7	ND.sup.d
CFP9	ND
CFP17	9251
CFP20	2388
CFP21	10732. . .

DETD [0432] The skin test activity of the purified proteins was tested in M. **tuberculosis** infected guinea pigs.

DETD [0433] 1 group of guinea pigs was infected via an ear vein with 1+10.sup.4 CFU of M. **tuberculosis** H37Rv in 0,2 ml PBS. After 4 weeks skin tests were performed and 24 hours after injection erythema diameter was. . .

DETD . . . significant Delayed Type Hypersensitivity (DTH) reaction.

TABLE 6

DTH erythema diameter in guinea pigs infected with 1 + 10.sup.4 CFU of M. **tuberculosis**, after stimulation with native antigens.

Antigen.sup.a	Skin reaction (mm).sup.b
Control	2.00

	PPD.sup.c	15.40 (0.53)
	CFP7	ND.sup.e
	CFP9	ND
	CFP17	11.25. . .

DETD . . . animal models.

TABLE 6a

DTH erythema diameter of recombinant antigens in outbred guinea pigs infected with 1 + 10.sup.4 CFU of M. **Tuberculosis**.

Antigen.sup.a	Skin reaction (mm).sup.b	
Control	2.9	(0.3)
PPD.sup.a	14.5	(1.0)
CFP 7a	13.6	(1.4)
CFP 17	6.8	(1.9)
CFP 20. . .		

DETD . . . and A.SW(H-2.sup.s) mice (Bomholtegaard, Ry) were given intravenous infections via the lateral tail vein with an inoculum of 5+10.sup.4 M. **tuberculosis** suspended in PBS in a vol. of 0.1 ml. 14 days postinfection the animals were sacrificed and spleen cells were. . .

DETD . . . female C57BL/6j(H-2.sup.b) mice (Bomholtegaard, Ry) were given intravenous infections via the lateral tail vein with an inoculum of 5+10.sup.4 M. **tuberculosis** suspended in PBS in a vol. of 0.1 ml. After 1 month of infection the mice were treated with isoniazid.

. . .	++	+++	+	
rCFP29	+++	+++	+++	++
rMPT51	+	-	-	-

Mouse IFN-γ release during recall of memory immunity to M. **tuberculosis**.

-: no response;
+: 1/3 of ST-CF;
++: 2/3 of ST-CF;
+++: level of ST-CF.

DETD . . . +++

rCFP21	+++
rCFP22	-
rCFP29	+
rCFP25	+++
rMPT51	+

Mouse IFN-γ release 14 days after primary infection with M. **tuberculosis**.

-: no response;
+: 1/3 of ST-CF;
++: 2/3 of ST-CF;
+++: level of ST-CF.

DETD . . . donors with no known exposure to patients with TB and from patients with culture or microscopy proven infection with Mycobacterium **tuberculosis**. Blood samples were drawn from the TB patients 1-4 months after diagnosis.

DETD [0472] 6 weeks after the last immunization the mice were aerosol challenged with 5+10.sup.6 viable Mycobacterium **tuberculosis** /ml. After 6 weeks of infection the mice were killed and the number of viable bacteria in lung and spleen. . .

DETD [0476] Species distribution of cfp7, cfp9, mpt51, rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b as well as of cfp7a, cfp7b, cfp10a, cfpl7, cfp21, cfp21, cfp22, cfp22a, cfp23, cfp25 and cfp25a.

DETD [0477] Presence of cfg7, cfp9, mpt51, rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b in different mycobacterial species.

DETD [0478] In order to determine the distribution of the cfp7, cfp9, mpt51, rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b genes in species belonging to the M. **tuberculosis**-complex and in other mycobacteria PCR and/or

Southern blotting was used. The bacterial strains used are listed in TABLE 10. Genomic. . .

DETD . . . were used in order to determine the distribution of the cfp7, cfp9 and mpt5l gene in species belonging to the **tuberculosis** -complex and in other mycobacteria. The bacterial strains used are listed in TABLE 10. PCR was performed on genomic DNA prepared. . .

DETD . . . bp). cfp9: stR3 and stF1 (351 bp).

TABLE 10

Mycobacterial strains used in this Example.

	Species and strain(s)	Source
1.	M. **tuberculosis**	H 3 7 R vATCC.sup.a (ATCC 27294)
2.		H 3 7 R aATCC (ATCC 25177)
3.		Erdman Obtained from A.

. . .

DETD . . . United Kingdom) with a vacuum transfer device (Milliblot, TM-v; Millipore Corp., Bedford, Mass.). The cfp7, cfp9, mpt51, rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b gene fragments were amplified by PCR from the plasmids pRVN01, pRVN02, pT052, pT087, pT088, pT089, pT090,. . .

DETD [0487] cfp7, cfp9 and mpt51 were found in the M. **tuberculosis** coinplex including BCG and the environmental mycobacteria; M. avium, M. kansasii, M. marinum, M. intracellular and M. flavescens. cfp9 was. .

DETD [0489] There is a strong band at around 26 kDa in M. **tuberculosis** H37Rv, Ra, Erdman, M. bovis AN5, M. bovis BCG substrain Danish 1331 and M. africanum. No band was seen in the region in any other tested mycobacterial strains.

TABLE 13a

Interspecies analysis of the rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b genes by Southern blotting.

Species and strain	rd1-orf2	rd1-orf3	rd1-orf4	**rd1-orf5**	rd1-orf8	rd1-orf9a	rd1-orf9b
1. M. tub. H37Rv	+	+	+	+	+	+	+
2. M. bovis	+	+	+	+	N.D.. . .		

DETD [0490] Positive results for rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b were only obtained when using genomic DNA from M. **tuberculosis** and M. bovis, and not from M. bovis BCG or other mycobacteria analyzed except rd1-orf4 which also was found in. . .

DETD [0492] Southern blotting was carried out as described for rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b. The cfp7a, cfp7b, cfploa, cfp17, cfp20, cfp21, cfp22, cfp22a, cfp23, cfp25 and cfp25a gene fragments were. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 1

LENGTH: 381

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 1

ggccgccggt acctatgtgg ccgccgatgc tgcggacgcg tcgacctata ccgggttctg 60

atcgaaccct gctgaccgag aggacttgtg atgtcgcaaa tcatgtacaa ctaccccgcg 120

atgttgggtc acgccgggga tatggccgga tatgccggca cgctgcagag. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 2

LENGTH: 96

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 2
Met Ser Gln Ile Met Tyr Asn Tyr Pro Ala Met Leu Gly His Ala Gly
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 3
LENGTH: 467
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 3
gggtagccgg accacggctg ggcaaagatg tgcaggccgc catcaaggcg gtcaaggccg 60
gcgacggcgt cataaacccg gacggcacct tgttggcggg ccccgcggtg ctgacgcccg 120
acgagtacaa ctcccggctg gtggccgccg acccggagtc caccgcggcg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 4
LENGTH: 108
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 4
Met Ala Ala Asp Pro Glu Ser Thr Ala Ala Leu Pro Asp Gly Ala Gly
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 5
LENGTH: 889
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 5
cgggtctgca cggatccggg ccgggcaggg caatcgagcc tgggatccgc tggggtgcgc 60
acatcgcgga cccgtgcgcg gtacggtcga gacagcggca cgagaaagta gtaagggcga 120
taataggcgg taaagagtag cgggaagccg gccgaacgac tcggtcagac. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 6
LENGTH: 162
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 6
Met Thr Asp Met Asn Pro Asp Ile Glu Lys Asp Gln Thr Ser Asp Glu
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 7
LENGTH: 898
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 7
tcgactccgg cgccaccggg caggatcacg gtgtcgacgg ggtcgccggg gaatcccacg 60
ataaccactc ttcgcgccat gaatgccagt gttggccagg cgctggcctg gcgtccacgc 120
cacacaccgc acagattagg acacgccggc ggcgcagccc tgcccgaaag. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 8
LENGTH: 165
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 8
Met Ala Gln Ile Thr Leu Arg Gly Asn Ala Ile Asn Thr Val Gly Glu
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 9
LENGTH: 1054
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 9
ataatcagct caccgttggg accgacctcg accaggggtc ctttgtgact gccgggcttg 60
acgcggacga ccacagagtc ggtcatcgcc taaggctacc gttctgacct ggggctgcgt 120
gggcgccgac gacgtgaggc acgtcatgtc tcagcggccc accgccacct. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 10
LENGTH: 217
TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 10
Met Thr Pro Arg Ser Leu Val Arg Ile Val Gly Val Val Val Ala Thr
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 11
LENGTH: 949
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 11
agccgctcgc gtggggtcaa ccgggtttcc acctgctcac tcattttgcc gcctttctgt 60
gtccgggccg aggcttgcgc tcaataactc ggtcaagttc cttcacagac tgccatcact 120
ggcccgtcgg cgggctcgtt gcgggtgcgc cgcgtgcggg tttgtgttcc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 12
LENGTH: 182
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 12
Met Ala Asp Cys Asp Ser Val Thr Asn Ser Pro Leu Ala Thr Ala Thr
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 13
LENGTH: 1060
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 13
tggaccttca ccggcggtcc cttcgcttcg ggggcgacac ctaacatact ggtcgtcaac 60
ctaccgcgac accgctggga ctttgtgcca ttgccggcca ctcggggccg ctgcggcctg 120
gaaaaattgg tcgggcacgg gcggccgcgg gtcgctacca tcccactgtg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 14
LENGTH: 219
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 14
Met Gly Ala Ala Ala Ala Met Leu Ala Ala Val Leu Leu Leu Thr Pro
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 15
LENGTH: 1198
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 15
cagatgctgc gcaacatgtt tctcggcgat ccggcaggca acaccgatcg agtgcttgac 60
ttttccaccg cggtgaccgg cggactgttc ttctcaccca ccatcgactt tctcgaccat 120
ccaccgcccc taccgcaggc ggcgacgcca actctggcag ccgggtcgct. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 16
LENGTH: 265
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 16
Met Asn Asn Leu Tyr Arg Asp Leu Ala Pro Val Thr Glu Ala Ala Trp
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 17
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: VARIANT
LOCATION: (1)
OTHER INFORMATION: Ala is Ala or Ser
SEQUENCE: 17
Ala Glu Leu Asp Ala Pro Ala Gln Ala Gly Thr. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 18

LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 18
Ala Gln Ile Thr Leu Arg Gly Asn Ala Ile Asn Thr Val Gly Glu
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 19
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: UNSURE
LOCATION: (3)
OTHER INFORMATION: Xaa is unknown
SEQUENCE: 19
Asp Pro Xaa Ser Asp Ile Ala Val Val Phe Ala Arg Gly. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 20
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 20
Thr Asn Ser Pro Leu Ala Thr Ala Thr Ala Thr Leu His Thr Asn
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 21
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: UNSURE
LOCATION: (2)
OTHER INFORMATION: Xaa is unknown
SEQUENCE: 21
Ala Xaa Pro Asp Ala Glu Val Val Phe Ala Arg Gly Arg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 22
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: UNSURE
LOCATION: (1)
OTHER INFORMATION: Xaa is unknown
SEQUENCE: 22
Xaa Ile Gln Lys Ser Leu Glu Leu Ile Val Val Thr Ala. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 23
LENGTH: 19
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 23
Met Asn Asn Leu Tyr Arg Asp Leu Ala Pro Val Thr Glu Ala Ala Trp
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 24
LENGTH: 34
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 24
cccggctcga gaacctstac cgcgacctsg cscc 34
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 25
LENGTH: 37
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 25

gggccggatc cgasgcsgcg tccttsacsg gytgcca 37
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 26
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 26
ggaagcccca tatgaacaat ctctaccg 28
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 27
LENGTH: 32
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 27
cgcgctcagc ccttagtgac tgagcgcgac cg 32
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 28
LENGTH: 24
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 28
ctcgaattcg ccgggtgcac acag 24
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 29
LENGTH: 25
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 29
ctcgaattcg cccccatacg agaac 25
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 30
LENGTH: 15
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 30
gtgtatctgc tggac 15
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 31
LENGTH: 15
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 31
ccgactggct ggccg 15
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 32
LENGTH: 24
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 32
gaggaattcg cttagcggat cgca 24
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 33
LENGTH: 15
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 33
cccacattcc gttgg 15
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 34
LENGTH: 15
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 34
gtccagcaga tacac 15
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 35
LENGTH: 27
TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 35
gtacgagaat tcatgtcgca aatcatg 27
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 36
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 36
gtacgagaat tcgagcttgg ggtgccg 27
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 37
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 37
cgattccaag cttgtggccg ccgacccg 28
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 38
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 38
cgttagggat cctcatcgcc atggtgttgg 30
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 39
LENGTH: 26
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 39
cgttagggat ccggttccac tgtgcc 26
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 40
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 40
cgttagggat cctcaggtct tttcgatg 28
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 41
LENGTH: 952
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 41
gaattcgccg ggtgcacaca gccttacacg acggaggtgg acacatgaag ggtcggtcgg 60
cgctgctgcg ggcgctctgg attgccgcac tgtcattcgg gttgggcggt gtcgcggtag 120
ccgcggaacc caccgccaag gccgccccat acgagaacct gatggtgccg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 42
LENGTH: 299
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 42
Met Lys Gly Arg Ser Ala Leu Leu Arg Ala Leu Trp Ile Ala Ala Leu
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 43
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 43
gcaacacccg ggatgtcgca aatcatg 27
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 44
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 44

gtaacacccg gggtggccgc cgacccg 27
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 45
LENGTH: 37
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 45
ctactaagct tggatcccta gccgccccat ttggcgg 37
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 46
LENGTH: 38
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 46
ctactaagct tccatggtca ggtcttttcg atgcttac 38
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 47
LENGTH: 450
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 47
gtgccgcgct ccccagggtt cttatggttc gatatacctg agtttgatgg aagtccgatg 60
accagcagtc agcatacggc atggccgaaa agagtggggt gatgatggcc gaggatgttc 120
gcgccgagat cgtggccagc gttctcgaag tcgttgtcaa cgaaggcgat. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 48
LENGTH: 71
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 48
Met Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 49
LENGTH: 750
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 49
gggtacccat cgatgggttg cggttcggca ccgaggtgct aacgcacttg ctgacacact 60
gctagtcgaa aacgaggcta gtcgcaacgt cgatcacacg agaggactga ccatgacaac 120
ttcacccgac ccgtatgccg cgctgcccaa gctgccgtcc ttcagcctga. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 50
LENGTH: 176
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 50
Met Thr Thr Ser Pro Asp Pro Tyr Ala Ala Leu Pro Lys Leu Pro Ser
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 51
LENGTH: 800
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 51
tcatgaggtt catcggggtg atcccacgcc cgcagccgca ttcgggccgc tggcgagccg 60
gtgccgcacg ccgcctcacc agcctggtgg ccgccgcctt tgcggcggcc acactgttgc 120
ttacccccgc gctggcacca ccggcatcgg cgggctgccc ggatgccgag. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 52
LENGTH: 226
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 52
Met Ile Pro Arg Pro Gln Pro His Ser Gly Arg Trp Arg Ala Gly Ala
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 53

LENGTH: 700
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 53
ctaggaaagc ctttcctgag taagtattgc cttcgttgca taccgccctt tacctgcgtt 60
aatctgcatt ttatgacaga atacgaaggg cctaagacaa aattccacgc gttaatgcag 120
gaacagattc ataacgaatt cacagcggca caacaatatg tcgcgatcgc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 54
LENGTH: 181
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 54
Met Thr Glu Tyr Glu Gly Pro Lys Thr Lys Phe His Ala Leu Met Gln
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 55
LENGTH: 950
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 55
tgggctcggc actggctctc ccacggtggc gcgctgattt ctccccacgg taggcgttgc 60
gacgcatgtt cttcaccgtc tatccacagc taccgacatt tgctccggct ggatcgcggg 120
taaaattccg tcgtgaacaa tcgacccatc cgcctgctga catccggcag. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 56
LENGTH: 262
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 56
Met Asn Asn Arg Pro Ile Arg Leu Leu Thr Ser Gly Arg Ala Gly Leu
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 57
LENGTH: 1000
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 57
cgaggagacc gacgatctgc tcgacgaaat cgacgacgtc ctcgaggaga acgccgagga 60
cttcgtccgc gcatacgtcc aaaagggcgg acagtgacct ggccgttgcc cgatcgcctg 120
tccattaatt cactctctgg aacacccgct gtagacctat cttctttcac. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 58
LENGTH: 291
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 58
Met Thr Trp Pro Leu Pro Asp Arg Leu Ser Ile Asn Ser Leu Ser Gly
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 59
LENGTH: 900
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 59
ttggcccgcg cgatcatcga aagccgttcg ggtgcggata ctttcggctc cgatggcggt 60
gagaagtgag ttttccgtat ttcatctcgc ctgagcaggc gatgcgcgag cgcagcgagt 120
tggcgcgtaa gggcattgcg cgggccaaaa gcgtggtggc gctggcctat. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 60
LENGTH: 248
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 60
Met Ser Phe Pro Tyr Phe Ile Ser Pro Glu Gln Ala Met Arg Glu Arg
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 61

LENGTH: 1560
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 61
gagtcattgc ctggtcggcg tcattccgta ctagtcggtt gtcggacttg acctactggg 60
tcaggccgac gagcactcga ccattagggt aggggccgtg acccactatg acgtcgtcgt 120
tctcggagcc ggtcccggcg ggtatgtcgc ggcgattcgc gccgcacagc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 62
LENGTH: 464
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 62
Met Thr His Tyr Asp Val Val Val Leu Gly Ala Gly Pro Gly Gly Tyr
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 63
LENGTH: 550
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 63
ggcccggctc gcggccgccc tgcaggaaaa gaaggcctgc ccaggcccag actcagccga 60
gtagtcaccc agtaccccac accaggaagg accgcccatc atggcaaagc tctccaccga 120
cgaactgctg gacgcgttca aggaaatgac cctgttggag ctctccgact. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 64
LENGTH: 130
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 64
Met Ala Lys Leu Ser Thr Asp Glu Leu Leu Asp Ala Phe Lys Glu Met
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 65
LENGTH: 900
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 65
tgaacgccat cgggtccaac gaacgcagcg ctacctgatc accaccgggt ctgttagggc 60
tcttccccag gtcgtacagt cgggccatgg ccattgaggt ttcggtgttg cgggttttca 120
ccgattcaga cgggaatttc ggtaatccgc tgggggtgat caacgccagc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 66
LENGTH: 228
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 66
Met Ala Ile Glu Val Ser Val Leu Arg Val Phe Thr Asp Ser Asp Gly
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 67
LENGTH: 500
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 67
gtttgtggtg tcggtggtct ggggggcgcc aactgggatt cggttggggt gggtgcaggt 60
ccggcgatgg gcatcggagg tgtgggtggt ttgggtgggg ccggttcggg tccggcgatg 120
ggcatggggg gtgtgggtgg tttgggtggg gccggttcgg gtccggcgat. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 68
LENGTH: 139
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 68
Met Gly Ala Gly Pro Ala Met Gly Ile Gly Gly Val Gly Gly Leu Gly
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 69

LENGTH: 2050
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 69
agcgcactct gagaggttgt catggcggcc gactacgaca agctcttccg gccgcacgaa 60
ggtatggaag ctccggacga tatggcagcg cagccgttct tcgaccccag tgcttcgttt 120
ccgccggcgc ccgcatcggc aaacctaccg aagcccaacg gccagactcc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 70
LENGTH: 666
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 70
Met Ala Ala Asp Tyr Asp Lys Leu Phe Arg Pro His Glu Gly Met Glu
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 71
LENGTH: 1890
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 71
gcagcgatga ggaggagcgg cgccaacggc ccgcgccggc gacgatgcaa agcgcagcga 60
tgaggaggag cggcgcgcat gactgctgaa ccggaagtac ggacgctgcg cgaggttgtg 120
ctggaccagc tcggcactgc tgaatcgcgt gcgtacaaga tgtggctgcc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 72
LENGTH: 591
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 72
Met Thr Ala Glu Pro Glu Val Arg Thr Leu Arg Glu Val Val Leu Asp
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 73
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 73
Asp Pro Val Asp Asp Ala Phe Ile Ala Lys Leu Asn Thr Ala Gly
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 74
LENGTH: 14
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: UNSURE
LOCATION: (14)
OTHER INFORMATION: Xaa is unknown
SEQUENCE: 74
Asp Pro Val Asp Ala Ile Ile Asn Leu Asp Asn Tyr Gly. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 75
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: UNSURE
LOCATION: (5)
OTHER INFORMATION: Xaa is unknown
SEQUENCE: 75
Ala Glu Met Lys Xaa Phe Lys Asn Ala Ile Val Gln Glu. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 76
LENGTH: 14
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:

NAME/KEY: VARIANT
LOCATION: (3)
OTHER INFORMATION: Ala is Ala or Gln
SEQUENCE: 76
Val Ile Ala Gly Met Val Thr His Ile His Xaa. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 77
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 77
Thr Asn Ile Val Val Leu Ile Lys Gln Val Pro Asp Thr Trp Ser
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 78
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 78
Ala Ile Glu Val Ser Val Leu Arg Val Phe Thr Asp Ser Asp Gly
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 79
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 79
Ala Lys Leu Ser Thr Asp Glu Leu Leu Asp Ala Phe Lys Glu Met
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 80
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: VARIANT
LOCATION: (4)
OTHER INFORMATION: Asp is Asp or Glu
SEQUENCE: 80
Asp Pro Ala Asp Ala Pro Asp Val Pro Thr Ala. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 81
LENGTH: 50
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 81
Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 82
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 82
Thr Thr Ser Pro Asp Pro Tyr Ala Ala Leu Pro Lys Leu Pro Ser
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 83
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 83
Thr Glu Tyr Glu Gly Pro Lys Thr Lys Phe His Ala Leu Met Gln
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 84
LENGTH: 15
TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 84
Thr Thr Ile Val Ala Leu Lys Tyr Pro Gly Gly Val Val Met Ala
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 85
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: UNSURE
LOCATION: (10)
OTHER INFORMATION: Xaa is unknown
SEQUENCE: 85
Ser Phe Pro Tyr Phe Ile Ser Pro Glu Xaa Ala Met Arg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 86
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 86
Thr His Tyr Asp Val Val Val Leu Gly Ala Gly Pro Gly Gly Tyr
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 87
LENGTH: 450
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 87
agcccggtaa tcgagttcgg gcaatgctga ccatcgggtt tgtttccggc tataaccgaa 60
cggtttgtgt acgggataca aatacaggga gggaagaagt aggcaaatgg aaaaaatgtc 120
acatgatccg atcgctgccg acattggcac gcaagtgagc gacaacgctc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 88
LENGTH: 98
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 88
Met Glu Lys Met Ser His Asp Pro Ile Ala Ala Asp Ile Gly Thr Gln
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 89
LENGTH: 460
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 89
gcaaccggct tttcgatcag ctgagacatc agcggcgtgc gggtcaacga cccacctgcg 60
ccaggtagcg actccgcgcg cagcaggccc gcgcccgcgc tggggcctga tccaccagcc 120
agcggatggt tcgacagcgg actggtgccg agcaggccca tctgcgcggc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 90
LENGTH: 139
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 90
Met Arg Val Asn Asp Pro Pro Ala Pro Gly Ser Asp Ser Ala Arg Ser
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 91
LENGTH: 1200
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 91
taataggccc ccaacacatc ggagggagtg atcaccatgc tgtggcacgc aatgccaccg 60
gagctaaata ccgcacggct gatggccggc gcgggtccgg ctccaatgct tgcggcggcc 120
gcgggatggc agacgctttc ggcggctctg gacgctcagg ccgtcgagtt. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 92

LENGTH: 371
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 92
Met Ile Thr Met Leu Trp His Ala Met Pro Pro Glu Leu Asn Thr Ala
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 93
LENGTH: 1000
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 93
gacgcgacac agaaatcctt aaggccggcg gccaaggggc cgaaggtgaa gaaggtgaag 60
ccccagaaac cgaaggccac gaagccgccc aaagtggtgt cgcagcgcgg ctggcgacat 120
tgggtgcatg cgttgacgcg aatcaacctg ggcctgtcac ccgacgagaa. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 94
LENGTH: 308
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 94
Met Lys Lys Val Lys Pro Gln Lys Pro Lys Ala Thr Lys Pro Pro Lys
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 95
LENGTH: 34
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 95
aagagtagat ctatgatggc cgaggatgtt cgcg 34
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 96
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 96
cggcgacgac ggatcctacc gcgtcgg 27
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 97
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 97
ccttgggaga tctttggacc ccggttgc 28
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 98
LENGTH: 25
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 98
gacgagatct tatgggctta ctgac 25
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 99
LENGTH: 33
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 99
ccccccagat ctgcaccacc ggcatcggcg ggc 33
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 100
LENGTH: 24
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 100
gcggcggatc cgttgcttag ccgg 24
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 101
LENGTH: 32

TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 101
ccggctgaga tctatgacag aatacgaagg gc 32
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 102
LENGTH: 24
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 102
ccccgccagg gaactagagg cggc 24
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 103
LENGTH: 38
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 103
ctgccgagat ctaccaccat tgtcgcgctg aaataccc 38
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 104
LENGTH: 25
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 104
cgccatggcc ttacgcgcca actcg 25
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 105
LENGTH: 32
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 105
ggcggagatc tgtgagtttt ccgtatttca tc 32
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 106
LENGTH: 25
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 106
cgcgtcgagc catggttagg cgcag 25
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 107
LENGTH: 32
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 107
gaggaagatc tatgacaact tcacccgacc cg 32
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 108
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 108
catgaagcca tggcccgcag gctgcatg 28
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 109
LENGTH: 33
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 109
ggccgagatc tgtgacccac tatgacgtcg tcg 33
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 110
LENGTH: 36
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 110
ggcgcccatg gtcagaaatt gatcatgtgg ccaacc 36
DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 111
LENGTH: 33
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 111
ccgggagatc tatggcaaag ctctccaccg acg 33
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 112
LENGTH: 32
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 112
cgctgggcag agctacttga cggtgacggt gg 32
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 113
LENGTH: 36
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 113
ggcccagatc tatggccatt gaggtttcgg tgttgc 36
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 114
LENGTH: 26
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 114
cgccgtgttg catggcagcg ctgagc 26
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 115
LENGTH: 24
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 115
ggacgttcaa gcgacacatc gccg 24
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 116
LENGTH: 24
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 116
cagcacgaac gcgccgtcga tggc 24
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 117
LENGTH: 26
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 117
acagatctgt gacggacatg aacccg 26
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 118
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 118
ttttccatgg tcacgggccc ccggtact 28
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 119
LENGTH: 26
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 119
acagatctgt gcccatggca cagata 26
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 120
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 120

tttaagcttc taggcgccca gcgcggc 27
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 121
LENGTH: 26
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 121
acagatctgc gcatgcggat ccgtgt 26
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 122
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 122
ttttccatgg tcatccggcg tgatcgag 28
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 123
LENGTH: 26
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 123
acagatctgt aatggcagac tgtgat 26
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 124
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 124
ttttccatgg tcaggagatg gtgatcga 28
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 125
LENGTH: 26
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 125
acagatctgc cggctacccc ggtgcc 26
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 126
LENGTH: 28
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 126
ttttccatgg ctattgcagc tttccggc 28
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 127
LENGTH: 50
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 127
Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 128
LENGTH: 49
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 128
Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 129
LENGTH: 50
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 129
Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val
1 5. . .
DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 130
LENGTH: 33
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 130
ccgggagatc tatggcaaag ctctccaccg acg 33
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 131
LENGTH: 32
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 131
cgctgggcag agctacttga cggtgacggt gg 32
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 132
LENGTH: 36
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 132
ggcgccggca agcttgccat gacagagcag cagtgg 36
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 133
LENGTH: 26
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 133
cgaactcgcc ggatcccgtg tttcgc 26
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 134
LENGTH: 32
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 134
ggcaaccgcg agatctttct cccggccggg gc 32
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 135
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 135
ggcaagcttg ccggcgccta acgaact 27
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 136
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 136
ggacccagat ctatgacaga gcagcagtgg 30
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 137
LENGTH: 47
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 137
ccggcagccc cggccgggag aaaagctttg cgaacatccc agtgacg 47
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 138
LENGTH: 44
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 138
gttcgcaaag cttttctccc ggccggggct gccggtcgag tacc 44
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 139
LENGTH: 20
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 139

ccttcggtgg atcccgtcag 20
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 140
LENGTH: 450
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 140
tggcgctgtc accgaggaac ctgtcaatgt cgtcgagcag tactgaaccg ttccgagaaa 60
ggccagcatg aacgtcaccg tatccattcc gaccatcctg cggccccaca ccggcggcca 120
gaagagtgtc tcggccagcg gcgatacctt gggtgccgtc atcagcgacc. . . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 141
LENGTH: 93
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 141
Met Asn Val Thr Val Ser Ile Pro Thr Ile Leu Arg Pro His Thr Gly
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 142
LENGTH: 480
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 142
ggtgttcccg cggccggcta tgacaacagt caatgtgcat gacaagttac aggtattagg 60
tccaggttca acaaggagac aggcaacatg gcaacacgtt ttatgacgga tccgcacgcg 120
atgcgggaca tggcgggccg ttttgaggtg cacgcccaga cggtggagga. . . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 143
LENGTH: 98
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 143
Met Ala Thr Arg Phe Met Thr Asp Pro His Ala Met Arg Asp Met Ala
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 144
LENGTH: 940
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 144
gccccagtcc tcgatcgcct catcgccttc accggccgcc agccgaccgc aggccacgtg 60
tccgccacct aacgaaagga tgatcatgcc caagagaagc gaatacaggc aaggcacgcc 120
gaactgggtc gaccttcaga ccaccgatca gtccgccgcc aaaaagttct. . . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 145
LENGTH: 261
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 145
Met Pro Lys Arg Ser Glu Tyr Arg Gln Gly Thr Pro Asn Trp Val Asp
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 146
LENGTH: 280
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 146
ccgaaaggcg gtgcaccgca cccagaagaa aaggaaagat cgagaaatgc cacagggaac 60
tgtgaagtgg ttcaacgcgg agaaggggtt cggctttatc gcccccgaag acggttccgc 120
ggatgtattt gtccactaca cggagatcca gggaacgggc ttccgcaccc. . . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 147
LENGTH: 67
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 147
Met Pro Gln Gly Thr Val Lys Trp Phe Asn Ala Glu Lys Gly Phe Gly

1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 148
LENGTH: 540
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 148
atcgtgtcgt atcgagaacc ccggccggta tcagaacgcg ccagagcgca aacctttata 60
acttcgtgtc ccaaatgtga cgaccatgga ccaaggttcc tgagatgaac ctacggcgcc 120
atcagaccct gacgctgcga ctgctggcgg catccgcggg cattctcagc. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 149
LENGTH: 129
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 149
Met Asn Leu Arg Arg His Gln Thr Leu Thr Leu Arg Leu Leu Ala Ala
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 150
LENGTH: 400
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 150
atagtttggg gaaggtgtcc ataaatgagg ctgtcgttga ccgcattgag cgccggtgta 60
ggcgccgtgg caatgtcgtt gaccgtcggg gccggggtcg cctccgcaga tcccgtggac 120
gcggtcatta acaccacctg caattacggg caggtagtag ctgcgctcaa. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 151
LENGTH: 110
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 151
Met Arg Leu Ser Leu Thr Ala Leu Ser Ala Gly Val Gly Ala Val Ala
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 152
LENGTH: 990
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 152
aatagtaata tcgctgtgcg gttgcaaaac gtgtgaccga ggttccgcag tcgagcgctg 60
cgggccgcct tcgaggagga cgaaccacag tcatgacgaa catcgtggtc ctgatcaagc 120
aggtcccaga tacctggtcg gagcgcaagc tgaccgacgg cgatttcacg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 153
LENGTH: 266
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 153
Met Thr Asn Ile Val Val Leu Ile Lys Gln Val Pro Asp Thr Trp Ser
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 154
LENGTH: 25
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 154
ctgagatcta tgaacctacg gcgcc 25
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 155
LENGTH: 35
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 155
ctcccatggt accctaggac ccgggcagcc ccggc 35
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 156

LENGTH: 29
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 156
ctgagatcta tgaggctgtc gttgaccgc 29
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 157
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 157
ctccccgggc ttaatagttg ttgcaggagc 30
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 158
LENGTH: 33
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 158
gcttagatct atgattttct gggcaaccag gta 33
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 159
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 159
gcttccatgg gcgaggcaca ggcgtgggaa 30
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 160
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 160
ctgagatcta gaatgccaca gggaactgtg 30
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 161
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 161
tctcccgggg gtaactcaga gcgagcggac 30
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 162
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 162
ctgagatcta tgaacgtcac cgtatcc 27
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 163
LENGTH: 27
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 163
tctcccgggg ctcacccacc ggccacg 27
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 164
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 164
ctgagatcta tggcaacacg ttttatgacg 30
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 165
LENGTH: 30
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 165
ctccccgggt tagctgctga ggatctgcth 30

DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 166
LENGTH: 31
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 166
ctgaagatct atgcccaaga gaagcgaata c 31
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 167
LENGTH: 31
TYPE: DNA
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 167
cggcagctgc tagcattctc cgaatctgcc g 31
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 168
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 168
Pro Gln Gly Thr Val Lys Trp Phe Asn Ala Glu Lys Gly Phe Gly
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 169
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: UNSURE
LOCATION: (15)
OTHER INFORMATION: Xaa is unknown
SEQUENCE: 169
Asn Val Thr Val Ser Ile Pro Thr Ile Leu Arg Pro Xaa. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 170
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
FEATURE:
NAME/KEY: VARIANT
LOCATION: (1)
OTHER INFORMATION: Thr could also be Ala
SEQUENCE: 170
Thr Arg Phe Met Thr Asp Pro His Ala Met Arg. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 171
LENGTH: 15
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 171
Pro Lys Arg Ser Glu Tyr Arg Gln Gly Thr Pro Asn Trp Val Asp
1 5 10. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 172
LENGTH: 404
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 172
Met Ala Thr Val Asn Arg Ser Arg His His His His His His His His
1 5. . .
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 173
LENGTH: 403
TYPE: PRT
ORGANISM: Mycobacterium **tuberculosis**
SEQUENCE: 173
Met Ala Thr Val Asn Arg Ser Arg His His His His His His His His
1 5. . .

CLM What is claimed is:

. . . in a) with respect to the ability of evoking a protective immune response against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex, or c) comprises an amino acid sequence having a sequence identity with the polypeptide defined in a) or the. . . in a) with respect to the ability of evoking a protective immune response against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex, with the proviso that i) the polypeptide fragment is in essentially pure form when consisting of the amino acid. . .

. . . weeks of primary infection or within 4 days after the mouse has been rechallenge infected with mycobacteria belonging to the **tuberculosis** complex, the induction performed by the addition of the polypeptide to a suspension comprising about 200.000 spleen cells per ml,. . . suspension; and/or 3) induces an IFN-γ release from bovine PBMC derived from animals previously sensitized with mycobacteria belonging to the **tuberculosis** complex, said release being at least two times the release observed from bovine PBMC derived from animals not previously sensitized with mycobacteria belonging to the **tuberculosis** complex.

. . . fragment as defined in any of claims 1-8, and an other polypeptide fragment derived from a bacterium belonging to the **tuberculosis** complex, such as ESAT-6 or at least one T-cell epitope thereof, MPB64 or at least one T-cell epitope thereof, MPT64. . .

. . . first amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. **tuberculosis** protein ESAT-6, and a second amino acid sequence including at least one T-cell epitope derived from a M. **tuberculosis** protein different from ESAT-6 and/or including a stretch of amino acids which protects the first amino acid sequence from in. . . first amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. **tuberculosis** protein MPT59, and a second amino acid sequence including at least one T-cell epitope derived from a M. **tuberculosis** protein different from MPT59 and/or including a stretch of amino acids which protects the first amino acid sequence from in. . .

. . . 11-13, wherein the at least one T-cell epitope included in the second amino acid sequence is derived from a M. **tuberculosis** polypeptide selected from the group consisting of a polypeptide fragment according to any of claims 1-55, DnaK, GroEL, urease, glutamine. . .

. . . sequence of ESAT-6 or of MPT59 and/or the second amino acid sequence is the amino acid sequence of a M. **tuberculosis** polypeptide selected from the group consisting of a polypeptide fragment according to any of claims 1-8, DnaK, GroEL, urease, glutamine. . .

. . . according to any of claims 1-20 in the preparation of a pharmaceutical composition for the diagnosis of or vaccination against **tuberculosis** caused by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis.

. . . been administered, the amount of expressed antigen being effective to confer substantially increased resistance to infections with mycobacteria of the **tuberculosis** complex in an animal, including a human being.

. . . according to claim 23 or 24 in the preparation of a pharmaceutical composition for the diagnosis of or vaccination against **tuberculosis** caused by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis.

35. A vaccine for immunizing an animal, including a human being, against

tuberculosis caused by mycobacteria belonging to the **tuberculosis** complex, comprising as the effective component a non-pathogenic microorganism, wherein at least one copy of a DNA fragment comprising a. . .
44. A transformed cell according to claim 43, which is a bacterium belonging to the **tuberculosis** complex, such as a M. **tuberculosis** bovis BCG cell.

. . . polypeptide from a short-term culture filtrate as defined in claim 1; or isolating the polypeptide from whole mycobacteria of the **tuberculosis** complex or from lysates or fractions thereof, e.g. cell wall containing fractions; or synthesizing the polypeptide by solid or liquid. . .
. . . of claims 1-20, and solubilizing or dispersing the polypeptide in a medium for a vaccine, and optionally adding other M. **tuberculosis** antigens and/or a carrier, vehicle and/or adjuvant substance, or cultivating a cell according to any of claims 37-45, and transferring. . .
48. A method of diagnosing **tuberculosis** caused by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis in an animal, including a human being, comprising intradermally injecting, in the animal, a polypeptide. . . composition according to claim 34, a positive skin response at the location of injection being indicative of the animal having **tuberculosis**, and a negative skin response at the location of injection being indicative of the animal not having **tuberculosis**
.

49. A method for immunising an animal, including a human being, against **tuberculosis** caused by mycobacteria belonging to the **tuberculosis** complex, comprising administering to the animal the polypeptide according to any of claims 1-20, the immunologic composition according to claim. . .
. . . A method for diagnosing ongoing or previous sensitization in an animal or a human being with bacteria belonging to the **tuberculosis** complex, the method comprising providing a blood sample from the animal or human being, and contacting the sample from the. . .
52. A composition for diagnosing **tuberculosis** in an animal, including a human being, comprising a polypeptide according to any of claims 1-20, or a nucleic acid. . .

L13 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:684968 CAPLUS
DN 129:300060
TI Novel antigens of Mycobacterium **tuberculosis** culture filtrates and the genes encoding and their diagnostic and prophylactic use
IN Andersen, Peter; Nielsen, Rikke; Rosenkrands, Ida; Weldingh, Karin; Rasmussen, Peter Birk; Oettinger, Thomas; Florio, Walter
PA Statens Serum Institut, Den.
SO PCT Int. Appl., 264 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 10

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9844119	A1	19981008	WO 1998-DK132	19980401
W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2285625	AA	19981008	CA 1998-2285625	19980401

PI AU 9868204 A1 19981022 AU 1998-68204 19980401
AU 740545 B2 20011108
EP 972045 A1 20000119 EP 1998-913536 19980401
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
JP 2001515359 T2 20010918 JP 1998-541074 19980401
EP 1449922 A2 20040825 EP 2004-76605 19980401
EP 1449922 A3 20041117
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY
CA 2319380 AA 19990520 CA 1998-2319380 19981008
WO 9924577 A1 19990520 WO 1998-DK438 19981008
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1029053 A1 20000823 EP 1998-947412 19981008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
NZ 504951 A 20010629 NZ 1998-504951 19981008
AU 750173 B2 20020711 AU 1998-94338 19981008
EP 1484405 A1 20041208 EP 2004-77071 19981008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY
PRAI DK 1997-376 A 19970402
US 1997-44624P P 19970418
DK 1997-1277 A 19971110
US 1998-70488P P 19980105
EP 1998-913536 A3 19980401
WO 1998-DK132 W 19980401
EP 1998-947412 A3 19981008
WO 1998-DK438 W 19981008

AB Culture filtrate antigens of Mycobacterium **tuberculosis** are characterized and cDNAs encoding them are cloned. Some of the proteins are antigenic and suitable for use in vaccines and in diagnosis of infections, e.g. skin tests. A fusion protein of two of these antigens is a superior immunogen compared to the unfused proteins. Individual antigens from culture filtrates were identified by T cell mapping using T cells from memory immune mice. Genes for individual antigens were then cloned by screening a λgt11 expression vector with monoclonal antibodies. Manufacture of individual antigens with hexahistidine affinity labels is described.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Novel antigens of Mycobacterium **tuberculosis** culture filtrates and the genes encoding and their diagnostic and prophylactic use

AB Culture filtrate antigens of Mycobacterium **tuberculosis** are characterized and cDNAs encoding them are cloned. Some of the proteins are antigenic and suitable for use in vaccines and in diagnosis of infections, e.g. skin tests. A fusion protein of two of these antigens is a superior immunogen compared to the unfused proteins. Individual antigens from culture filtrates were identified by T cell mapping using T cells from memory immune mice. Genes for individual antigens were then cloned by screening a λgt11 expression vector with monoclonal antibodies. Manufacture of individual antigens with hexahistidine affinity labels is described.

ST Mycobacterium culture filtrate antigen gene; vaccine **tuberculosis** Mycobacterium antigen gene

IT Lipoproteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(19 kDa, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and

prophylactic use)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(85 complex, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Chaperonins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DnaK, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ESAT6, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Chaperonins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GroEL, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Chaperonins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GroES, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MPT51, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MPT59, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MPT64, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Antigens
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(culture filtrate antigens of Mycobacterium; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT **Tuberculosis**
(diagnosis, vaccines against and diagnosis of; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Escherichia
Mycobacterium
Mycobacterium BCG
Pseudomonas
Salmonella
(expression host for Mycobacterium **tuberculosis** antigen genes; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(for antigens of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Hemagglutinins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heparin-binding, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Antibodies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, to antigens of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Mycobacterium **tuberculosis**
(novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Molecular cloning
(of antigen genes of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Fusion proteins (chimeric proteins)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(of antigens of Mycobacterium **tuberculosis**, for vaccines; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Protein sequences
(of antigens of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT DNA sequences
(of genes for antigens of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors
(pRVN01, expression vector for antigen genes of Mycobacterium **tuberculosis** on; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors
(pRVN02, expression vector for antigen genes of Mycobacterium **tuberculosis** on; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors
(pTO87, gene for antigen of Mycobacterium **tuberculosis** on; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors
(pTO88, gene for antigen of Mycobacterium **tuberculosis** on; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors
(pTO89, gene for antigen of Mycobacterium **tuberculosis** on; novel antigens of Mycobacterium **tuberculosis** culture

filtrates and genes encoding and their diagnostic and prophylactic use)
IT Plasmid vectors
(pTO90, gene for antigen of Mycobacterium **tuberculosis** on; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)
IT Plasmid vectors
(pTO91, gene for antigen of Mycobacterium **tuberculosis** on; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)
IT Plasmid vectors
(pTO96, gene for antigen of Mycobacterium **tuberculosis** on; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)
IT Plasmid vectors
(pTO98, gene for antigen of Mycobacterium **tuberculosis** on; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)
IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphate-binding, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)
IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(proline-rich, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)
IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rd1-orf2, for antigen of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)
IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rd1-orf3, for antigen of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)
IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rd1-orf4, for antigen of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)
IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**rd1-orf5**, for antigen of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)
IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rd1-orf8, for antigen of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)
IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rd1-orf9a, for antigen of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rdl-orf9b, for antigen of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Antibodies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(to antigens of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Mycobacterium africanum
Mycobacterium bovis
(**tuberculosis** caused by; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Diagnosis
(**tuberculosis**, vaccines against and diagnosis of; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Vaccines
(**tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT **Tuberculosis**
(vaccines against and diagnosis of; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Crystallins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α-, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT 213992-07-5 213992-08-6 213992-09-7D, amino acid-substituted analogs
213992-10-0 213992-11-1 213992-12-2 213992-13-3 213992-14-4
213992-15-5 213992-16-6 213992-17-7 213992-18-8 213992-19-9
213992-20-2 213992-21-3 213992-22-4 213992-23-5 213992-24-6
214072-43-2 214072-44-3 214072-45-4 214072-46-5 214072-47-6
214142-58-2
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(N-terminal peptide of Mycobacterium **tuberculosis** antigen; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT 151185-45-4, Protein (Mycobacterium BCG strain Tokyo ribosome)
208778-78-3 208782-67-6 208783-23-7 208783-90-8 208786-90-7
208788-06-1 208788-47-0 208790-41-4 208790-42-5 208853-48-9
208856-86-4 208857-49-2 208859-77-2 208863-45-0 208864-30-6
208865-40-1 208868-63-7 208871-19-6 208872-79-1 208874-21-9
208875-49-4 209053-74-7 210170-05-1 214348-60-4 214348-78-4
214348-84-2 214348-92-2 214349-12-9 214349-22-1 214349-24-3
214349-26-5 214349-38-9
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT 9002-13-5D, Urease, fusion products 9023-70-5D, Glutamine synthetase, fusion products 9029-06-5D, Alanine dehydrogenase, fusion products 9054-89-1D, Superoxide dismutase, fusion products
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as antigen of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT 214348-46-6 214348-59-1 214348-61-5 214348-62-6 214348-68-2
214348-69-3 214348-70-6 214348-76-2 214348-77-3 214348-79-5
214348-80-8 214348-81-9 214348-82-0 214348-83-1 214348-85-3
214348-86-4 214348-88-6 214348-89-7 214348-90-0 214348-91-1
214348-93-3 214349-11-8 214349-21-0 214349-23-2 214349-25-4
214349-28-7 214349-47-0 214349-53-8 214349-54-9 214349-57-2
214349-60-7 214349-62-9 214349-63-0
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)